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VOLUME 2
1919

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AMERICAN MEDICAL ASSOCIATION
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VOLUME 2 NUMBER 1

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PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $5.00

Entered as second-class matter January 7, 1919, at the postoffice at Chicago, Illinois, under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103, Act of October 3, 1917, authorized Jan. 15, 1919.

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HISTOPATHOLOGIC STUDY ON TWO CASES OF "CENTRAL NEURITIS"; DEMONSTRATION OF A NEW GRANULE ("NUCLEOPROTEID-LIKE GRANULE") IN THE NEUROGLIA CELLS *

KIYOYASU MARUI, M.D.
SENDAI, JAPAN

INTRODUCTION

Since Dr. Adolf Meyer[1] described, in 1901, the symptom-complex "central neuritis," which he introduced as a short designation of the "parenchymatous systemic degeneration mainly in the central nervous system," a number of cases have been added to the literature by different authors, and there is no doubt that this condition can be recognized from its clinical symptoms and established anatomically. According to the descriptions of authors, this symptom-complex is found to occur in depressive psychoses at the time of involution, in alcoholic senile states and in alcoholic phthisical-cachectic states, and the clinical condition is characterized by diarrhea, emaciation, twitchings and rigidity of the extremities, some fever and some changes in the reflexes, and the mental condition is an anxious, perplexed agitation, delirium or stupor. Anatomic investigation revealed "changes somewhat similar to those found in the motor cells of the cord and the medulla, from which the nerve process has been cut off at the periphery" in the Betz cells and other cells, and systemic degenerations of the central nerve fibers. Beside the accurate description of Dr. Meyer, there are a number of excellent histologic studies on changes of the nerve cells; however, we find relatively few investigations on alteration of the neurofibrils of nerve cell as well as the neuroglia tissue. The material of the Phipps Clinic recently offered the opportunity to study two cases of "central neuritis." The alteration of the intracellular neurofibrils of nerve cells as the effect of cutting off the nerve process has been a topic of several experimental studies. In view of the clear relationship of the changes of the nerve cells in

* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, the Johns Hopkins Hospital, Baltimore.

1. Meyer, Adolf: On the Parenchymatous Systemic Degeneration Mainly in the Central Nervous System, Brain, Lond. **24**: 1901.

"central neuritis" and the axonal alteration resulting from section of fiber, an investigation of the appearance of the neurofibrils may be of value, as "central neuritis" is, so to speak, an experiment of nature, although the nerve process is not really cut off. Thorough investigation of the changes of the neuroglia tissue led me to demonstration of a new granule in neuroglia cells, a finding which may throw a new light on the problems of the metabolism and catabolism process of the central nervous tissue.

Before taking up the description of my investigation, I beg to express my highest appreciation of the kindness of Dr. Adolf Meyer, who gave me the privilege of studying these cases and many other specimens of our laboratory, and also gave me many useful suggestions in this study.

ILLUSTRATIVE CASES

CASE 1.—*Clinical History.*—E. B., a housewife, aged 29, in January, 1918, presented the skin lesion of pellagra, constipation, epigastric distress, and restlessness. Admitted to the medical service May 25, she showed marked emaciation and peculiar very dark pigmentations over the entire body. She became delirious May 29, and was transferred to our clinic. She developed a stupor and a typical picture of "central neuritis," with tenseness, rigidity, tetanoid positions and jactitations, and a terminal temperature of 107 F.

Family History.—A sister has nervous headaches, the daughter has tantrums and night terrors; an aunt broke down after the death of her husband.

Personal History.—The patient had the childhood diseases, typhoid fever at 16 and rheumatic fever at 20. Her development was abnormal; she married at 19 against her parents' wishes. Her married life was uneventful except for a miscarriage at 20 and an abortion at 28. The patient's habits have been regular, but the diet consisted mostly of vegetables. She has two children.

Present Illness.—In November, 1916, she began to become irritable. A spontaneous abortion in March, 1917, with hemorrhage for three months increased this condition and weakened her. She recovered somewhat during the summer, but in September, 1917, restlessness, night sweats, and her old symptoms returned. By December, 1917, she was worse, easily upset and much worried when her younger child developed scarlet fever. In January, 1918, epigastric distress, giddiness, flashes of light, and roughening of the hands appeared, and grew gradually worse. She took to bed on March 13; two days later her temperature was 101 F. and she had difficulty in swallowing. The last two symptoms left her March 16, and on light diet and rest she gradually improved till May 8, being out of bed she showed thirst, tachycardia, sleeplessness and a return of the other symptoms. On May 25 she was admitted to the medical service of the Johns Hopkins Hospital, with her hands in the condition described. Her mouth and tongue were sore; she was emaciated, very weak, slightly anemic, and her skin was dry and darkly pigmented. She was mentally clear until May 29, when she had an episode of screaming and confusion. On May 30 she was at times disoriented, frightened and was incontinent. On May 31 she was completely disoriented, delirious and incontinent. Her temperature was 101.5 F., and the pulse 140.

Mental Status.—The patient lay in bed twisting her hands and face, picking at the bed clothes and moving her jaw frequently. She mutters unintelligibly. Her arms and legs are rigid in flexion. She is usually unresponsive. She is completely disoriented and in the medical service had imagined she was giving birth to a baby. Incontinence.

Physical Status.—The patient is extremely emaciated; her skin harsh and dry and diffusely pigmented. On the backs of her hands and front of wrists and on the knuckles there is a dry, cracked, raised, very dark thickening of the skin symmetrically distributed. She is pale, her tongue red with swollen papillae; pyorrhea and dental caries. Tenseness and rigidity of musculature, and limbs in flexion, very hyperactive deep reflexes.

Progress in Clinic.—After admission in our clinic the patient grew continually worse; she muttered to herself, became more rigid and more restless, slept none and appeared to have slight spasms with retraction of the head. Later she was unable to swallow. Her temperature rose to 107 F., on June 2. Her pulse rose to 180 and Biot's breathing appeared. She died June 3.

Necropsy.—No macroscopical lesion in the brain and in the spinal cord; the microscopic study revealed "central neuritis."

CASE 2.—*Clinical History.*—A. S., widow, aged 48. Dating from September, 1917, the patient was nervous and weak. Dilatation and curettement operation followed by delirious state. On admission (December, 1917) the patient showed amebic dysentery with suspicion, hallucinations of hearing, disorientation, delusions and fear. This mental state kept pace wth her physical dilapidation, which rapidly led to exitus.

Family History.—Unimportant.

Personal History.—Negative. The patient felt "run down" and weak for the past year, without, however, any failure in business activities. In November, 1917, the patient appeared very weak; kept in bed for two weeks and on Nov. 17, 1917, a D. and C. operation was done with prolonged response to anesthetic. Following the operation the patient was agitated and suspicious of food. When she tried to jump out of the window she was transferred to a sanitarium. The patient developed diarrhea, six to seven stools a day, watery and bloody; she was very weak and during the last three days prior to admission she was tube-fed.

On admission the patient seemed confused and disoriented and profoundly exhausted. For a time she was restless, showing sudden paroxysms as though in pain. The knees were flexed and the abdominal muscles felt contracted. During the attacks she rolled from side to side in the bed; but between the attacks she seemed relaxed and quiet.

Physical Status.—The patient is a profoundly undernourished, emaciated anemic-looking woman. The neurologic examination showed definite exaggeration of deep reflexes. The abdomen is boat-shaped; the patient holds the muscles tense. Stool examination revealed the existence of *Ameba histolytica.* The patient began to run a temperature after three days in the hospital, ranging between 99 and 101 F.

Mental Status.—The patient thought her food was poisoned and she refused food, so that tube feeding was at times required. She also sometimes talked vaguely of being married to a Dr. Adams. She also had auditory hallucinations. The patient was usually oriented to time and place, but had difficulty in getting names straight. Retention and memory for remote past were good. She showed no definite affective disturbances.

Progress in the Clinic.—The diarrhea continued throughout the course in the hospital with from one to seventeen stools a day. The temperature ranged between 99 and 101 F. The above mentioned mental state continued till the end of January, 1918, interrupted now and then by remissions, in which she was fairly well oriented and showed no delusions. On January 31, marked twitchings of facial muscles and tremor of the lips were noticed.

From the beginning of February, 1918, the patient's condition appeared worse; the weakness increased and nausea and vomiting came on after meals. Defecation and micturition often occurred involuntarily. On February 13 the temperature rose from 101 to 104, and the pulse to 140. The patient became semicomatose and died.

Necropsy.—The brain showed superficially normal findings; microscopic study established typical "central neuritis."

MICROSCOPIC FINDINGS

(A) *Manifestations of the Nerve Cells.*—In both cases of "central neuritis" the paracentral lobule and the anterior central gyrus were subjected to a most extensive study. The spinal cord was examined only in the first case. To avoid repetition I shall describe below the findings of both cases together, and besides mention only points of difference between two cases.

We shall begin with the description of the findings in thionin preparations. So far as the cytoarchitecture of the cortex is concerned, both cases showed nothing abnormal. Almost all the Betz cells are in both cases in a more or less advanced stage of axonal reaction. The cell body is more or less swollen, and shows in a certain place an area of an almost homogeneous character due to a decay of the stainable substance into dust-like particles. In the extremely altered cell, the latter looks like a more or less deeply blue stained balloon. In the second case we find fairly well preserved stainable portions in the dendrites and also lumps of the Nissl bodies at the periphery of some cells, forming a rim around the margin. The "whirlpool" arrangement of the Nissl bodies, described by Dr. Meyer,[1, 2] did not come to our observation in this case. In the first case the superimposed fever alteration complicated the characteristic features; even at the periphery of the cells and in the dendrites the Nissl bodies have disappeared and the protoplasm is stained diffusely blue. The nucleus is found more or less dislocated in every cell usually to the side or toward the neighborhood of apical dendrite, causing sometimes a projection of the cell surface. The nucleus itself is sometimes round, sometimes it looks elongated or distorted and flattened, as if pressed to the wall by the swollen portion of the cell. The nuclear membrane is usually sharply marked, the content is pale,

2. Meyer, Adolf: Demonstrations of Various Types of Changes in the Giant Cell of the Paracentral Lobule, Am. J. Insan. **54**: 1897.

the nucleolus is round and generally deeply stained. Along the margin of the swollen cell or sometimes accumulated in one point of the cell there appears a heap of yellowish, greenish pigment. Figure 1 was taken from a Betz cell of the second case.

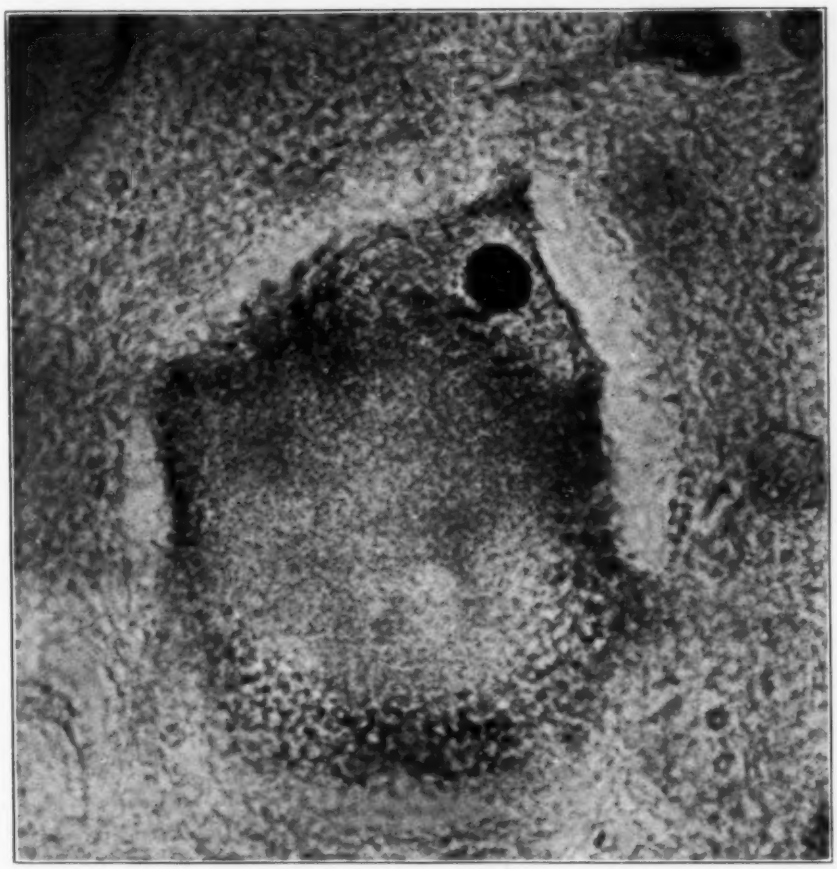

Fig. 1.—A Betz cell from the second case.*

In our first case some of the pyramidal cells of outer layers also show axonal reaction; however, most of them give an entirely different picture. They are mostly swollen; the dendrites are also enlarged. The Nissl bodies had largely disappeared from the cell body; no dislocation of the nucleus was noticed. The whole picture corresponds to that which Goldscheider and Flatau described as the effect of arti-

*Figures 1 to 6 are photomicrographs and Figures 7 to 9 were drawn with the use of the Abbe camera lucida with slight rotation of the micrometer screw.
Figures 1, 5, 6, 8 and 9 are thionin preparations.

ficial increase of body temperature. We also found some shrinkage cells (so designated by Hoch[3]) in the second and third layers.

In the second case the medium-sized and small pyramids also show a close resemblance to Hoch's shrinkage cells; the "alteration with rarefication around the nucleus" of Hoch was also found in some of the larger pyramids. The thionin preparations of alcohol material show practically the same picture as the above described preparation of formalin material.

A portion of the motor cells of the spinal cord and some of the cells of the Clark column show in our first case typical axonal reaction, although in less advanced stages, and some of them show, moreover, the fever alteration. Some other cells show merely fever alteration.

The manifestations of the intracellular neurofibrils of the nerve cells were studied in Bielschowsky preparations. Cotton and Southard[4] found in their Cajal and Bielschowsky preparations a definite change in the fibrils within the chromatolyzed area. Lambert[5] observed a disappearance of the fibrils exactly corresponding to the area of swelling in the Nissl equivalent. Figure 2 shows the alteration of the fibrils and the nerve cell; with the lower magnification the Betz cells appear as swollen bodies with sharply marked dendrites, and thus reminds us of the bed-bugs. In higher magnification we can follow different stages of the neurofibril alteration in different cells. The fibrils are in more or less advanced stages of fragmentation, and in the extreme state they are dissolved to fine dust-like pieces. In the central part of the cell body, where thionin preparations show an homogeneous area, we find also in the Bielschowsky stain a glossy area; however, at the periphery of the cell body and also in the dendrites, in which thionin stain disclosed well marked Nissl bodies, we find fairly well preserved neurofibrils, sometimes running from one dendrite to another. In the apical dendrite of the Betz cells the neurofibrils are especially clearly demonstrated and run isolated or in bundles toward the cell body. It is a striking feature that these neurofibrils end sharply at the base of the dendrite. These findings are very interesting, as they tend to indicate that the alteration of the neurofibrils keep pace with the dissolution of the Nissl bodies. As a

3. Hoch, August: Nerve Cell Changes in Somatic Diseases, Am. J. Insan. **55**: 1889.

4. Cotton, H. A., and Southard, E. E.: A Case of Central Neuritis with Autopsy, Am. J. Insan. **65**: 1908.

5. Lambert, C. I.: Notes on Pathological Material, N. Y. State Hosp. Bull. **1**: No. 3, 1908.

Fig. 2.—Bielschowsky stain; a Betz cell from the second case. The nucleus is found on the left-hand side of the cell; the pigment is found on the right-hand margin of the cell.

further evidence of this phenomenon may serve the Bielschowsky preparation of our first case; here we do not find any neurofibrils in most of the Betz cells even at the periphery of the cell body and the dendrites and thionin stain disclosed, as already remarked, dissolution of the Nissl bodies in the same. This corresponds to the statement of Lambert,[5] who observed more or less apparent fragmentation and granulation of the fibrils in the fever change. Marinesco[6] stated that the changes in the neurofibrils and the chromatophil elements as a rule occur and progress together. Dr. Meyer[7] and Lambert consider the changes in the fibrils almost invariably coincident with the changes of the local protoplasm. The Bielschowsky preparation of the spinal cord in our first case brought out samples of axonal reaction in the anterior horn and the Clark column; but owing to the superimposed fever alteration the neurofibrils are marked only in a few cells at the cell periphery and in the dendrites.

(B) *Manifestations of the Nerve Fibers and the Axis-Cylinders.*—The Marchi preparations showed definite myelin-sheath degeneration in the marrow of the paracentral lobules and the anterior central convolutions; however, the degenerated myelin-sheaths are so scanty that only a few appear in one Marchi section in both of our cases (Fig. 3). The Marchi cross-section of the spinal cord of our first case shows a number of degenerated fibers in the anterior and lateral pyramidal (Fig. 4) bundles as well as the cerebellar afferent bundles; but the degeneration in the pyramidal bundles is much slighter than the findings in the paracentral lobule and the anterior central convolution would make one expect; Dr. Meyer[1] and others also noticed this incongruity.

The Alzheimer-Mann preparations of the anterior central convolutions disclosed a very interesting finding in both of our cases (Fig. 7). In this preparation normal axis-cylinders are brought out in a deeply blue stain; but among those we find axis-cylinders with red-stained parts of different length in their course. Some fibers show colorless parts instead of the red-stained part. Between the red-stained part and blue-stained part of the fiber we find sometimes a very short colorless part, and sometimes we observe that the red-stained part is interrupted by colorless parts in many segments. Some axis-cylinders have in their course more than one red-stained or colorless part, so that they look like strings of changing color. It admits no doubt

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6. Marinesco: Lesions of the Neurofibrils in Certain Pathological Conditions, Rev. Neurol and Psychiat., 1905.

7. Meyer, Adolf: Discussion of the Data Concerning Neurofibrils, with Illustrations, Proceedings New York Neurol Soc., Feb. 6, 1906. J. Nerv. & Ment. Dis. **33**: 1906.

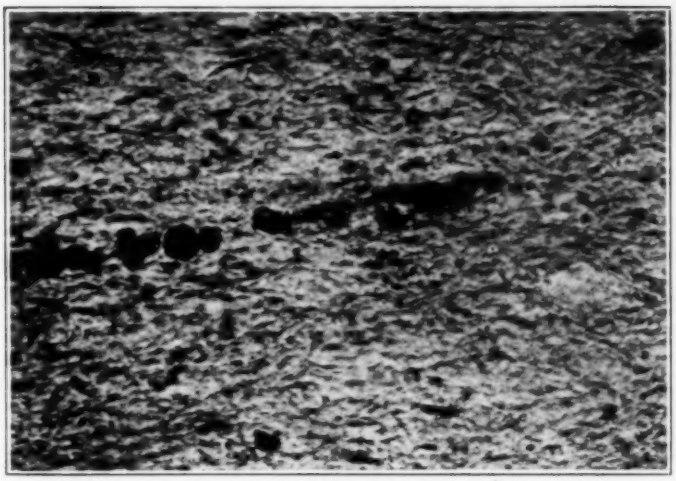

Fig. 3.—Marrow of the anterior central convolution (first case). Marchi's stain.

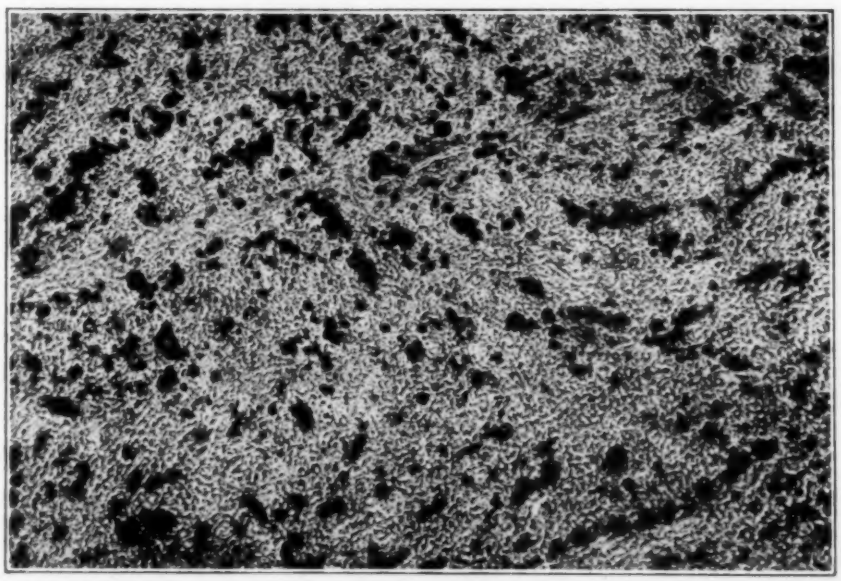

Fig. 4.—Cross-section of the lateral pyramidal bundle (first case). Marchi's stain.

that these red-stained and colorless segments of the fibers are degenerated, and that the red-stained parts are in a more advanced state of alteration than the colorless parts. Now it is worthy of note, that these degenerated axis-cylinders were found in the sections much more numerous than the degenerated myelin-sheaths demonstrated by the Marchi method. The Alzheimer-Mann stain of the longitudinal sections of the cord in our first case revealed many such degenerating axis-cylinders in the lateral pyramidal bundles and in the cerebellar afferent bundles.

On the basis of the fact, that in acute cases the cell change far outweighs the fiber degeneration, Cole[8] claimed that the former are almost certainly primary, and the latter appear to be simply a secondary manifestation of the former. But considering the possibility that the degeneration of the myelin sheaths may be demonstrable by the Marchi method in different parts of their course in different fibers, as Turner[9] suggested, and that the axis-cylinders are altered, even when the Marchi degeneration is absent, I am of the same opinion as Turner, that the degeneration of the fibers is sufficient to account for the state of the Betz cells.

The longitudinal section of the spinal cord, stained with thionin showed another interesting picture in some of the fibers of the lateral pyramidal bundles and the cerebellar afferent bundles. As Figure 6 indicates, those fibers show in their course variously long stretches of a deeply blue stain, inserted between colorless parts of the fibers. These blue-stained segments of the fibers hold their stain even if the differentiation by alcohol is pushed further, and to my mind they correspond to the red-stained segments of the fibers in the Alzheimer-Mann preparation described above, and are to be interpreted as degenerated portions of the fibers.

(C) *Manifestations of the Neuroglia Tissue.*—In cases of "central neuritis" an increase of satellite cells as well as of free nuclei was described by Dr. Meyer,[1] Lambert,[5, 10] Sims[11] and others. Our first case showed only moderate increase of satellite cells around the Betz cells and some of the pyramidal cells, but the second case did not give the picture of satellitosis. Lambert[10] observed nests of neuroglia

8. Cole, S. J.: On Changes in the Central Nervous System in the Neuritic Disorders of Chronic Alcoholism, Brain, Lond. **25**: 1902.

9. Turner, J.: An Account of the Nerve Cells in Thirty-Three Cases of Insanity, Brain, Lond. **26**: 1903.

10. Lambert, C. I.: Demonstrations of Pathological Anatomical Cases, N. Y. State Hosp. Bull. **2**: No. 3, 1909.

11. Sims, R.: Anatomical Findings in Two Cases of Korsakow's Symptom-Complex, J. Nerv. & Ment. Dis. **32**: 1905.

Fig. 5.—Longitudinal section of the cerebellar afferent bundle of the spinal cord (first case).

cells, in which from twenty-five to fifty were closely crowded together, and he said that they multiply by direct division. Similar nests of from three to fifteen neuroglia cells were found in both of our cases (Fig. 8*a*). As Lambert[10] suggested, they rarely show mitosis, and I also think they divide in the way of amitosis, partly at least.

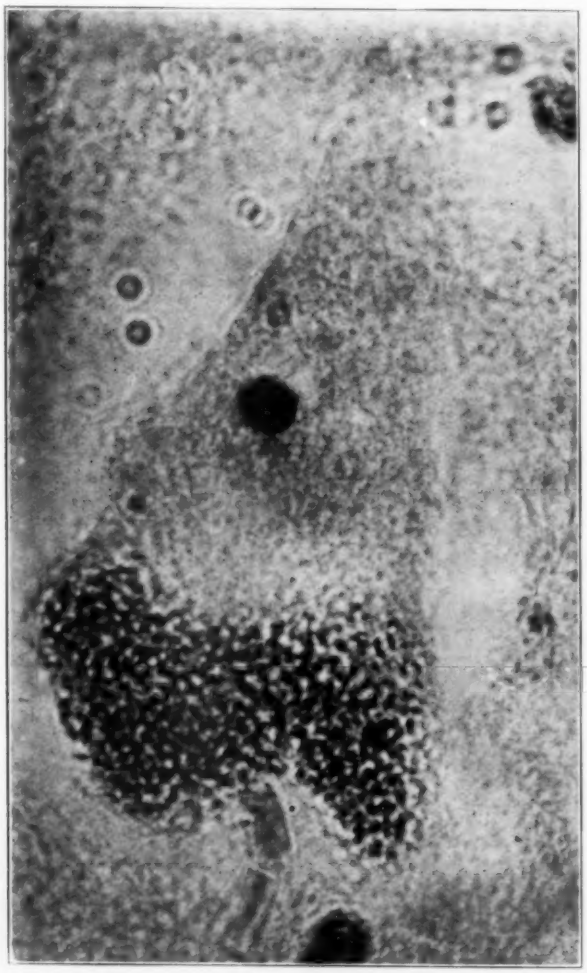

Fig. 6.—A Betz cell after pancreatin digestion.

Special attention was paid to the so-called catabolism process and the catabolism products. In both cases we observed the production of a number of ameboid glia cells, carrying different kinds of granules, which will be described later. Young ameboid glia cells show relatively small amounts of protoplasm, while larger and older ones have

much protoplasm and also protoplasm processes. Keeping pace with the appearance of these ameboid glia cells we find regressive changes of the neuroglia nuclei; these are: homogeneous stain of the nuclei, dilapidation of the nuclei into small spherules and pale stain with evidence of swelling. It is worthy of special note that in our second case we found a large number of neuroglia cells, the nuclei of which are quite small and round and deeply and diffusely blue stained with thionin, and containing a large deeply blue-stained nucleolus (Fig. 8 *a*, *b*). These nuclei are mostly surrounded by a certain amount of greenish, yellowish pigment, which evidently belongs to the cell body of the neuroglia cells. I think that these nuclei are also in a state of regressive alterations.

Prior to the description of ameboid glia cells, I should like to call attention to an interesting appearance of the neuroglia cells in the marrow of the paracentral lobule. As Figure 8 *d* shows, thionin preparation disclosed many spindle-shaped cells, the long axis of which runs parallel with the nerve fibers in the marrow. The nuclei of these cells are oval or oblongate and deeply blue stained, and have a deeply blue stained large nucleolus; the cell body is also diffusely blue stained or sometimes it shows a honey-comb appearance and tapers off at both ends. From each end of this spindle cell there extends a varicose more or less dark blue-stained fiber. The whole picture gives the impression that the glia cell is lying on an altered nerve fiber. This impression is strengthened, when we study the Mallory, Mann and Alzheimer preparations. In all these preparations we find in the marrow of the paracentral lobule many a spindle-shaped cell with a homogeneously stained oblong or oval nucleus containing a large nucleolus. The relation of the cell and the underlying nerve fiber is clearer in these preparations, because the latter is demonstrated clearly. The cell protoplasm of this spindle cell carries different kinds of granules, which will be described later. It will be noted here that in the spinal cord section of our first case the same spindle-shaped glia cells lying on the nerve fiber were observed in the pyramidal bundle and the cerebellar afferent bundle. I think that this finding is identical with the picture shown in Alzheimer's[12] Text Figure 3 A. Ameboid glia cells were found in both of our cases in the cortex as well as in the marrow, often forming a group independently or in the neighborhood of the blood vessels. Also in the spinal cord of the first case I found a large number of ameboid glia cells.

12. Alzheimer, A.: Beiträge zur Kenntnis der pathologischen Neuroglia und ihrer Beziehungen zu den Abbauvorgängen im Nervengewebe, Histolog. u. Histopatholog. Arbeiten 3, 1910.

The ameboid glia cells with large protoplasm show one or multiple vacuoles of different sizes, which may be well explained as fat cysts; the Herxheimer stain revealed red stained, variably large fat drops around the neuroglia nuclei. The Mallory and the Mann preparations showed in a relatively small number of the ameboid glia cells and the above described spindle-shaped glia cells the Alzheimer methyl blue granules. The Alzheimer fuchsin light green preparations, however, demonstrated in a large number of both kinds of the cells the fuchsinophil granules. The Alzheimer light green granules never did come to our observation; nor did the fibrinoid granules come to observation in our Weigert's neuroglia preparations. Besides the methyl blue and fuchsinophil granules the thionin preparations brought to light in a large number of the ameboid glia cells another kind of granule, to which we wish to devote the next chapter.

THE "NUCLEOPROTEID-LIKE GRANULE" IN THE NEUROGLIA CELLS

The granule referred to was demonstrated in the protoplasm of ameboid glia cells in the marrow and also (a little less) in the cortex. Our second case of "central neuritis" showed much more numerous cells with this granule. Besides the ameboid glia cells with large cell body, we found the same granule also in those glia cells, which have a more or less large cell body, but not the characteristic shape of an ameba (preameboid glia cell Rosenthal[13]). The grouping of the granules is quite different due to the different shapes of the cell body; sometimes we find granules all around the nucleus, and sometimes we find them either on one side or on both sides of the nucleus. Here and there we meet groups of granules without showing the neuroglia nuclei, especially often in the neighborhood of blood vessels; they are evidently sections of cell body or protoplasm processes of the glia cells, carrying the granules; according to my observation the latter never lie freely in the tissue or in the perivascular spaces.

The granule is round, or has the shape of an irregular lump; it is rather small and of almost uniform size. It appears in the thionin preparation of both formalin and alcohol fixed materials in a blue stain or in an exquisite metachromatic color, and between the blue stained and the metachromatic basophil stained ones there appear granules with many transition colors (Fig. 8 *a*, *c*). In the illumination by electric light they are especially brilliantly visible, and even the blue-stained granules glisten with a more or less metachromatic tinge.

13. Rosenthal, S.: Experimentelle Studien über amöboide Umwandlung der Neuroglia, Referat. Ztschr. f. d. gesamt. Neurol. u. Psychiat. Referat. u. Ergebnisse **8**: 1914.

Moreover, the electric illumination disclosed the same granules even in the spindle-shaped glia cells described above, the protoplasm of which appeared in a diffusely blue stain in the daylight. The whole picture of the granules is thus far similar to the granules which I[14] observed in the ameboid glia cells in the synapse of the Mauthner cell in fatigue. As I was not able at that time to study the solubility of that granule, I identified it with the Alzheimer basophil metachromatic granule, which Alzheimer himself identified with Reich's granule on the basis of its morphologic character. The Reich granule is characterized as soluble in warm alcohol at 45 C., ether and in warm xylol. The question now arises whether our granule is identical with the Reich granule, because our specimen showed the granule despite the fact that it had gone through warm xylol in process of embedding. The present cases furnish sufficient material to investigate the microchemical nature of our granule. The fact that we find the granule in the embedded specimens speaks from the first rather against the probability of its being a fat or lipoid substance. Paraffin sections from 2 to 10μ thick were placed in alcohol (80 per cent., 95 per cent., and absolute), ether, equal mixture of ether and absolute alcohol, chloroform xylol and turpentine oil, and kept in a water bath at 70 C. for from one to three hours, and then were stained with thionin in the same way as the control sections from the same block. Microscopic examination showed no definite decrease in the amount of granules.

Acetic acid (diluted as well as concentrated), concentrated hydrochloric acid, nitric acid and sulfuric acid were applied to sections for two to three hours; however, they did not affect the characteristic stainability of our granule. On the other hand, our granule is quite easily soluble in diluted as well as concentrated alkaline solution; 0.5 per cent. aqueous solution of sodium hydrate dissolves the granule in a short time.

A very interesting picture for the microchemical characterization of our granule was given by the digestion experiment. Paraffin sections from 2 to 6μ thick were digested by pepsin hydrochloric acid solution at 37 C. for from twelve to eighteen hours. The ground substance of the protoplasm of ameboid glia cells was dissolved, whereas our granule remained undigested around the nuclei, and much more distinctly visible after the digestion. Moreover, it is interesting to note that the granule showed the metachromatic color much more beautifully after the digestion, and it is noteworthy that the granules,

14. Marui, K.: The Effect of Overactivity on the Morphological Structure of the Synapse, J. Comp. Neurol. **31**: 1919.

which appeared in a more or less blue tinge before the digestion, showed an exquisite metachromatic color after the experiment.

Extremely interesting is the fact that in the experiments thus far described our granules behave microhistochemically in quite the same manner as the Nissl bodies of the nerve cells; as Held[15] described in 1895, the Nissl substance was dissolved only in alkaline solution as in our experiments, but not in different kinds of acid, in fat-solving mediums, and by pepsin. The only difference consists in the fact that our granules are demonstrated in a more or less brilliant metachromatic color, whereas the Nissl bodies appear in a more blue violet color.

Now, as Held[15] observed, the Nissl bodies show an exquisitely granular structure, if we look at very thin sections (2μ thick). The granules are round and do not look much larger than our granules in the neuroglia cells, and show a more or less metachromatic tinge, especially in electric illumination. After pepsin digestion they appear in a very characteristic metachromatic color in the thionin stain, just as some of our granules in the neuroglia cells. I cannot give a definite explanation to this interesting phenomenon; the fact does, however, indicate further evidence that both granules resemble each other. For the further characterization of our granules I undertook pancreatin digestion of sections. Paraffin sections, from 2 to 6μ thick, were placed in a neutral pancreatin solution for several hours at 38 C., and then they were stained in the ordinary way. Contrary to the result of pepsin digestion the granules of the neuroglia cells in the cortex as well as in the marrow disappeared entirely. The cortex gave a peculiar picture after this procedure; as Figure 6 shows, the Nissl bodies are entirely gone, and we can locate the nerve cells only by the existence of the yellowish pigment and also by the appearance of the nuclei. After five hours' digestion the nuclei of the nerve cells and the glia cells were stained rather distinctly and the nucleoli of the nerve cells were stained pale. Hence, in this point too, our granule reacts microchemically in the same way as the Nissl substance. The microhistochemical reaction of phosphoric acid was done following the direction of Lilienfeld and Monti;[16] our granule and the Nissl substance showed a slightly positive reaction, as they appeared in a brownish, yellowish color.

Judging from all the results thus far described, I came to the conclusion that our granule in the neuroglia cells has chemically a close relation to the Nissl substance. Since the thorough microchemical

15. Held, H.: Beiträge zur Struktur der Nervenzellen und ihrer Fortsatze. Arch. f. Anat. u Physiol. Anat., Abt., 1895.

16. Lilienfeld and Monti: Ueber die mikrochemische Lokalisation des phosphors in den Geweben, Ztschr. f. physiol. Chem. **17**: 1893.

Fig. 7. — Marrow of the anterior central convolution (second case); Alzheimer-Mann's stain.

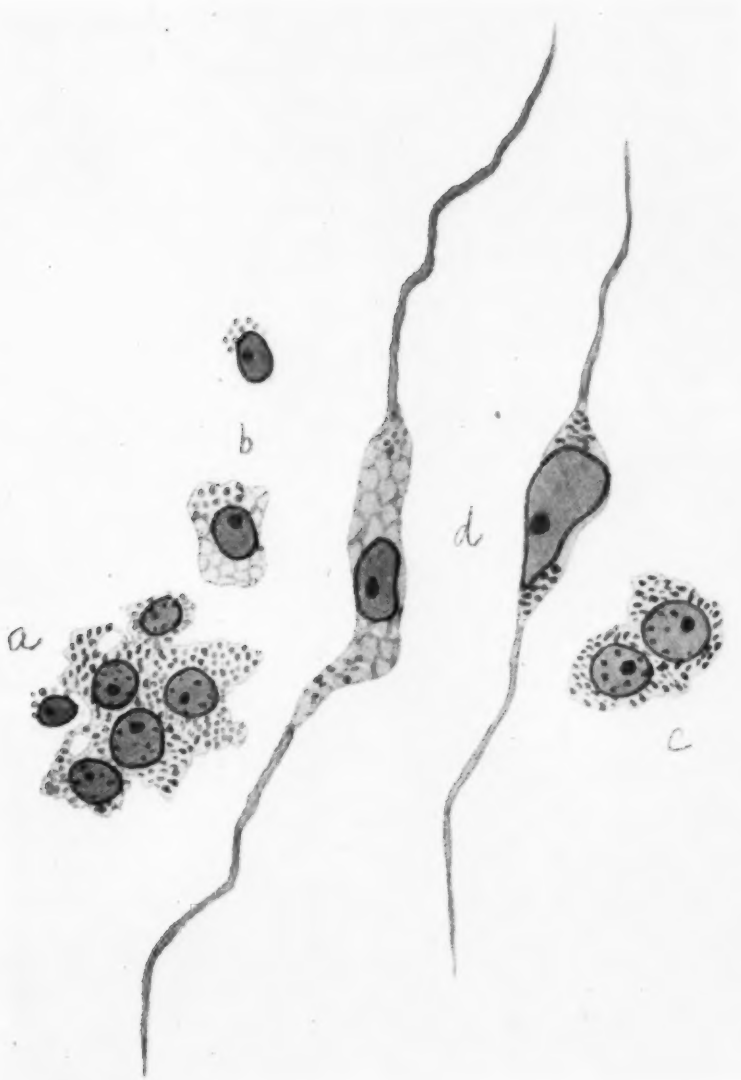

Fig. 8.—Different manifestations of neuroglia cells in "central neuritis" cases.

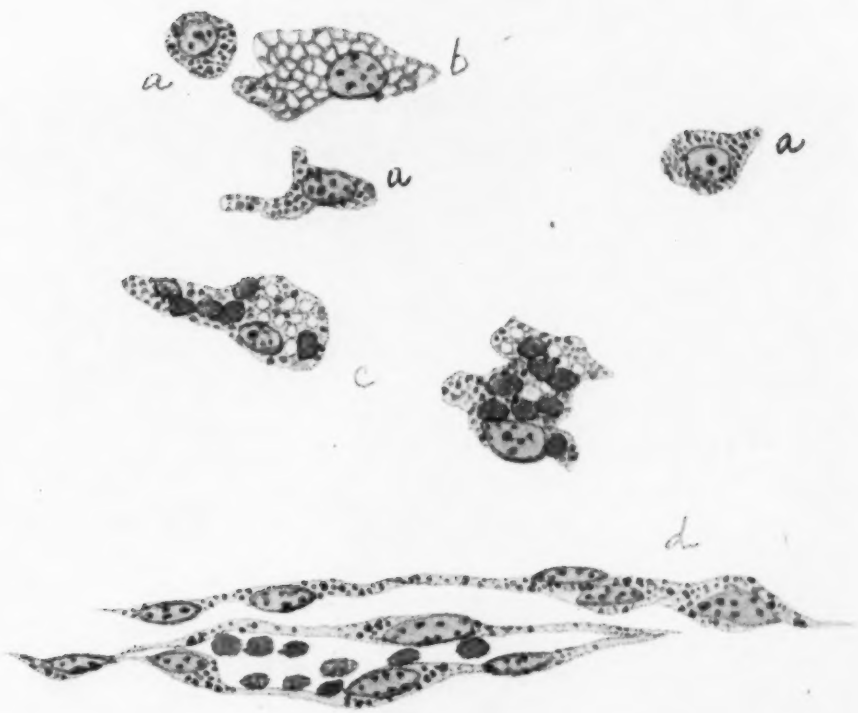

Fig. 9.—Granule cells and blood vessels in a small fresh hemorrhage.

study of Held on the Nissl substance there is no doubt that the latter belongs to the category of nucleoproteid; so I would like to designate our granule as "nucleoproteid-like granule" in the neuroglia cell. There is no doubt then that our granule is chemically quite different from the Reich π-granule; I therefore made a mistake when I identified the granule in the ameboid glia cells found in the synapse of the Mauthner cell in fatigue with the Alzheimer basophil metachromatic granule (Reich's $\dot{\pi}$-granule). In what relation our granule stands with the so-called "albumin-like granule," which was found in the granule cells in the brains of new-borns, and on which there was a controversy between Virchow[17, 18] and Jastrowitz,[19] I do not know. As far as I can see, the only fact known about that granule is that it is soluble in alkaline solution; a further study is required to decide this question. It is also doubtful now whether the Alzheimer basophil metachromatic granule is really identical with the Reich granule. He described his granule as stained in a metachromatic color, and as especially visible in electric illumination; but these properties are not specific for the Alzheimer granule nor for the Reich granule, as our granule has the same qualities. Alzheimer admitted, moreover, that the morphology of his granule is somewhat different from that of the Reich granule, and also that the solubility condition appeared to him a little different. He stated that his granule decreased distinctly by putting the section in alcohol. So this question also must be reserved for further investigation. At least, we can state that a metachromatic stain and electric illumination do not by any means suffice for the characterization of his granule.

Under the heading of "simple basophil catabolism substances," Alzheimer[12] described several basophil substances, which show no, or very little, tendency to metachromatic stain. His description is somewhat vague. He characterized one of them through the fact that (1) it is demonstrated only in alcohol sections, not in formalin material; (2) it is found in nerve cells, in neuroglia cells and also in groups in the perivascular spaces, and (3) it is demonstrated much more in the cortex than in the marrow. This granule is quite different from our granule in many respects. Another kind of basophil products of Alzheimer (Table 33, Fig. 3) is found, according to him, in the neuroglia cells, especially in the marrow, and demonstrated in the shape of lumps. To my mind, this granule resembles somewhat our

17. Virchow, R.: Encephalitis Congenita, Berl. klin. Wchnschr., No. 46, 1883.

18. Virchow, R.: Verhandlungen d. Berlin med. Gesellschaft. Sitzung. v. 14 Oktober, 1883, Berl. klin. Wchnschr., No. 46, 1883.

19. Jastrowitz: Diskussion zu den Vorträgen von Jacusiel u. Virchow in den Sitzungen der medizinischen Gesellschaft, Berl. klin. Wchnschr., No. 46, 1883.

granule, but I am far from being able to say that they are both the same thing. As already remarked, sometimes our granule is demonstrated in a basophil stain, showing little tendency to metachromasia. So I must declare that whenever we speak of the latter kind of the Alzheimer "basophil catabolism product," we have to exclude first in a microchemical way our "nucleoproteid-like" granule. As far as I know, our granule is quite new, at least in so far as its chemical nature is determined.

Then the question comes, whether our granule is connected with any specific morbid condition of the central nervous system and how frequently we meet this kind of granule in the neuroglia cells. Through the kindness of Dr. Meyer, I was given the privilege of studying many specimens in our laboratory; in all, I went over thionin preparations of seventy cases, mostly taken from the paracentral lobule. The cases belonged to both insane and general hospital cases, and the age of the patients ranged from 2 weeks to 68 years. To my surprise, I found the same granule very easily in twenty cases, and with some effort in twenty-five cases and none in the rest. Generally speaking, the granule was demonstrated in typical ameboid glia cells or in glia cells, the protoplasm of which is more or less larger than usual (preameboid glia cells Rosenthal?), in the cortex as well as in the marrow. So far as my observation went, I could not make out any specific cause for the appearance of the granule. As a most interesting finding I emphasize here that in a case of aplastic anemia, I found in and around a small fresh hemorrhage in the corpus callosum a large number of granule cells loaded fully with the "nucleoproteid-like granules." Newly produced granule cells have round or more or less simple shapes, and do not show any basket-like structure of their cell body; the latter is filled with the granules. Those young granule cells, which have a more or less irregular shape, have a close resemblance with ameboid glia cells (Fig. 9, *a*). On the other hand, the granule cells show an exquisite tendency to form basket-like structures, and I observed all the transition forms between the young granule cells and the typical basket-like granule cells; in other words, we found many cells with both basket-like structure and a more or less large protoplasm rest. Extremely interesting was the finding of the nucleoproteid-like granules in this protoplasm rest and in the ribs between the basket meshes (Fig. 9, *a, b, c*). There were also found many phagocytic cells in the hemorrhage, which contained many red blood corpuscles in their cell body. Especially noteworthy was here as well the finding of the same granules between those red blood corpuscles. These findings are very interesting in so far as a new chemically well-defined granules were observed in granule cells. The

question whether these granule cells have something to do with those granule cells in the brains of new-borns is to be decided by further investigation. The cells of blood vessels show in and around this hemorrhage very distinct progressive manifestations. We observed new production of cells of blood vessels, which show a tendency to form mesodermal granule cells and also to form new capillaries. These cells all carry in their protoplasm the same "nucleoproteid-like granules" (Fig. 9 *d*). In two cases of "central neuritis" we observed the granules only here and there in the protoplasm of swollen adventitia cells of blood vessels, around which many ameboid cells with different granules were found crowded. Herxheimer's stain showed variously large fat drops in the ameboid glia cells, as well as in cells of the adventitia. The question, whether the "nucleoproteid-like granule" appears only in certain morbid conditions of the central nervous tissue, or whether it is a normal constituent of neuroglia cells, which is found increased in quantity in morbid conditions, I cannot answer definitely at present. Although I found this granule in brains, which showed no definite histopathologic manifestation, except for the fact that the neuroglia cells had a more or less larger protoplasm body, we can never be sure in our necropsy material that we are dealing with absolutely normal brains. It would be necessary to add here that in two "normal" sheep brains I did not observe any neuroglia cell with this granule.

BIOLOGIC SIGNIFICANCE OF THE "NUCLEOPROTEID-LIKE GRANULE" IN THE NEUROGLIA CELLS

Since the thorough study of Alzheimer[12, 20] on the pathologic neuroglia, we know that in certain pathologic conditions the neuroglia tissue produces ameboid glia cells, which work as scavengers of catabolism products of the central nervous tissue. Alzheimer[12] described several catabolism products with different morphologic character and staining reaction. His methyl blue granule is produced according to him from the protoplasm of cells, which are bound to rapid decay, and dissolved and transformed into fat substance by mesodermal cells and carried away. Rosenthal,[13] who wanted to explain the production of the methyl blue granule as a sign of necrobiosis of neuroglia tissue, regarded the appearance of the fuchsinophil granule as that of an increased scavenger activity. So there is no doubt, that in our cases of "central neuritis" ameboid glia cells are

20. Alzheimer, A.: Ueber die Abbauvorgänge im Nervensystem. Referat auf d. VII Jahresversammlung der Gesellschaft Deut. Nervenärzte un Breslau, Sept., 1913, Deutsch. Ztschr. f. Nervenh. **50**: 1914.

working as scavenger of catabolism products. The "simple basophil catabolism product" was interpreted by Alzheimer as a manifestation of a characteristic dissolution process of cell protoplasm. The so-called basophil metachromatic granule has, according to Alzheimer, something to do with myelin, although he was in doubt whether the granule comes from decay or nutrition disturbance of myelin fibers. But the biologic significance of these granules is to my mind to be considered after their nature becomes clearer by further investigation. What then is the biologic significance of our "nucleoproteid-like granule"? Could it also be attributed to catabolism products in the same sense as that of Alzheimer? This is by no means an easy question to answer definitely. That our granule has microchemically a close resemblance to the Nissl granule, I described conclusively above. Now many investigations indicate a close relation between the Nissl substance and nuclear substance with regard to their histological character. Holmgren,[21] Sjöval[22] and I[14] also expressed the opinion that on the occasion of tigrolysis the Nissl substance is regenerated from the nucleus; according to Scott, the Nissl substance comes out of the nucleus during the development of the nerve cell. On the other hand, it is known that in reparative activity of root ganglion cells (after section of the nerve cell process) and in specific nervous activity (fatigue) we always observe a change of the chromophil substance. Heidenhain[23] said that this substance is accumulated in the rest state, whereas in activity it undergoes specific metamorphosis and produces specific energy. It is then highly improbable that our granule, which is chemically closely related to such an important substance, should be given to ameboid glia cells and other cells as a catabolism product of the nervous tissue. Also the fact that our granule is found in larger quantity in the marrow than in the cortex, speaks rather against this view. The postmortem appearance of ameboid and preameboid glia cells was studied by Buscaino,[24] Rosenthal[13] and Wohlwill,[25] but it is hard to conceive a postmortem production of our granule. Then, we must appeal to another possibility — whether our granule is given to neuroglia cells in an afferent

21. Holmgren, E.: Studien in der feineren Anatomie der Nervenzellen, Anatomische Hefte **15**: 1900.

22. Sjövall, E.: Die Nervenzellenveränderungen bei Tetanus und ihre Bedeutung, Jahrbuch. f. Psychiat. u. Neurol. **23**: 1903.

23. Heidenhain, M.: Plasma und Zelle, I$_2$, 1911.

24. Buscaino, V. M.: Sulle genesi e Sul significato delle cellule amoeboidi. Referat. Ztschr. f. d. gesamt. Neurol. u. Psychiat. Referate u. Ergebnisse, **8**: 1914.

25. Wohlwill: Ueber amoeboide Glia, Virchow's Arch. **216**: 1914.

direction; in other words, from blood, and is eventually related to a reparative or reconstructive and also nutritive process of the nerve tissue. The finding of the same granule in cells of blood vessels may afford a point of support to this assumption, although we do not know in what chemical form it is given and in what chemical process it is produced in the cells.

Extremely interesting is the finding of the "nucleoproteid-like granule" in granule cells. Merzbacher[26] studied the morphology and biology of granule cells, to which he gave the designation "Abräumzellen"; among the granule cells, which are found in embryonic brains, he distinguished two categories: "physiological granule cell" ("embryologische Auffauzellen") and "Abräumzellen" in a narrower sense ("granulare metamorphosiete Gliazellen"). He said in his conclusion: "There is no decided difference between the "Abräumzellen" and "Auffauzellen"; they both have the property to take material and work it out and to pass it on. The distinction between the two comes into consideration when we follow the fate of the material, which was given to the cells. In the one case it is carried away, and at another time it is used for the production of a new substance and structure. The study of Wlassak[27] on embryonic material strongly suggests the activity of neuroglia during the evolution of the nerve tissue. De Montet[28] regarded the myelin as the expression of import and construction as well as of catabolism process. It is, then, perhaps not going too far to assume that in certain pathologic conditions and nutrition disturbances of nerve tissue other chemical substances besides fat substance may be given to the latter by the neuroglia tissue. Moreover, it is easy to understand that the nerve tissue needs some protein substance besides fat as its constructive and nutritive substance. To my mind our granule belongs to this kind of substance. The further question, whether this substance is given as such or if it is also given, after it is changed into some other substances, I shall leave undecided. According to Wlassak the origin of myelin is to be sought in the blood. While fat production from protein substance is decidedly denied by several physiologic chemists (Schenck, Gürber), others (Kunze) spoke for this possibility up to quite recently. Arnold

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26. Merzbacher, L.: Untersuchungen über die Morphologie u. Biologie der Abräumzellen im Zentralnervensystem, Histolog. u. Histopatholog. Arbeiten **3**: 1909.

27. Wlassak: Die Herkunft des Myelins, Arch. f. Entwicklingsmechn. d. Organ. **4**: 1898.

28. De Montet: Ueber Wanderungen lipoider Substanzen im Centralnervensystem, Inaugural Dissertation z. Erlangung d. med. Doktorwürde d. hohen med. tak. d. Universität Bern, 1906.

and Dietrich considered that in certain pathologic conditions fat production from protein substance is possible but not proved. Jakob[29] also admitted the possibility of production of lipoid catabolism products from axis-cylinders, which go to decay. Our findings also seem to indicate the same possibility, but we cannot consider this is proved. As already remarked, we found in granule cells and ameboid glia cells fat cysts beside the "nucleoproteid-like granule"; but it is always possible that they give one substance on the one hand and take the other on the other hand. In some glia cells we also found yellowish, greenish pigment beside the granule; but I do not know whether this pigment was present before or newly produced, because Obersteiner[30; 31] showed the existence of this pigment in neuroglia cells of normal brains increasing in quantity with age. Marinesco and Sander assumed the production of pigment of nerve cells from the Nissl substance; Obersteiner regarded it as a residuum of metabolism processes of the nerve cell. In what relation our finding stands with the assumption of these authors I do not know.

So I came to the conclusion that the neuroglia tissue not only has the function of scavenger through production of granule cells and ameboid glia cells in certain pathologic conditions and nutrition disturbances, but also the function of "Auffau" in the sense of Merzbacher.

SUMMARY

The results of a thorough histopathologic study in two cases of "central neuritis" and many other cases can be summarized as follows:

1. Almost all the Betz cells in both cases and some cells of the spinal cord of the first case showed the typical axonal reaction; in the first case the fever alteration was superimposed upon this picture.

2. Fragmentation of the intracellular neurofibrils was found in the glassy area; the alteration of neurofibrils keeps pace with the dissolution of the Nissl bodies.

3. Besides Marchi degeneration of myelin sheaths, a very interesting picture of degenerated axis-cylinders was disclosed.

4. Ameboid glia cells showed the Alzheimer fuchsinophil granule, a finding which indicates an increased scavenger activity of the neuroglia tissue.

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29. Jakob, A.: Ueber die feinere Histologie der sekundären Faserdegeneration in der weissen Substanz des Rückenmarks (mit besonderer Berücksichtigung der Abbauvorgänge), Histolog. u. Histopatholog. Arbeiten 5$_1$, 1912.

30. Obersteiner, H.: Ueber das hellgelbe pigment in den Nervenzellen und das Vorkommen weiterer fettähnlicher Körper im Centralnervensystem, Arbeiten a. d. Neurol. Institut. **10**: 1903.

31. Obersteiner, H.: Weitere Bemerkungen über die Fettpigmentkörnchen im Centralnervensystem, Arbeiten a. d. Neurol. Institut. **11**: 1904.

5. In two cases of central neuritis and many other cases in ameboid and preameboid glia cells on the one hand, and in a case of hemorrhage in granule cells on the other hand, a new "nucleoproteid-like granule" was demonstrated and a conclusion was drawn that neuroglia has a constructive function besides a scavenger function, and that this granule is given the neuroglia cells in an afferent direction.[32]

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32. In addition to the references already given, the following will be found of interest:

Reich, F.: Ueber eine Granulation in den Nervenzellen, Arch. f. Anat. u. Physiol., Physiolog. Abt., 1903.

Reich, F.: Ueber die feinere Struktur der peripheren Nerven, Ztschr. f. Psychiat. **62**: 1905.

Reich, F.: Ueber den zelligen Aufbau der Nervenfaser auf Grund mikrohistiochemischer Untersuchungen, J. f. Psychol. u. Neurol. **8**: 1906-1907.

Somers, E. M.: Central Neuritis, New York State Hosp. Bull. **1**: No. 3, 1908.

A CONTRIBUTION TO THE HISTOPATHOLOGY OF EPIDEMIC ("LETHARGIC") ENCEPHALITIS*

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The various symptoms of epidemic ("lethargic") encephalitis—somnolence, stupor with or without slight elevation of temperature, together with ocular and other cranial nerve paralyses, etc., may occur in many cerebral disorders. We may mention the hemorrhagic superior polioencephalitis of Wernicke, the cerebral form of poliomyelitis, the sleeping sickness caused by trypanosomiasis, syphilitic meningitis, paretic dementia, encephalitis caused by anthrax (Fulci[1]) or other infectious diseases, as tuberculosis, cerebrospinal meningitis and especially influenza. Here also belong cases of poisoning with carbon monoxid, sulphuric acid (Wernicke[2]) and meat and fish (botulism). Any of the types of encephalitis mentioned may so resemble the clinical picture and course of the epidemic ("lethargic") form that they, undoubtedly, have been and are confounded with the latter. Especially striking is the clinical similarity between lethargic encephalitis and the sleeping sickness caused in man by the *Trypanosoma gambiense*, hence "lethargic" encephalitis is popularly called "sleeping sickness." In addition, from our histopathologic studies of three cases of so-called lethargic encephalitis we are forced to the conclusion that the latter, though a disease *sui generis, does not differ histologically from the African sleeping sickness due to trypanosome infection.*

Of the three cases here described, two have been briefly reported by one of us (Bassoe[3]) and a third case, in a baby 4 weeks old, came under observation of Drs. C. G. Grulee and Peter Bassoe not long ago.

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* From the laboratories of pathology of Cook County and Psychopathic Hospitals, Chicago.

* Read before the Section on Nervous and Mental Diseases at the Seventieth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1919.

1. Fulci, F.: Die acute hämorrhagische Leptomeningo-enzephalitis bei der Milzbrandinfektion des Menschen, Nissl-Alzheimer's Arbeiten **6**:161, 1913.
2. Wernicke, C.: Lehrbuch der Gehirnkrankheiten **2**:229, 1881, Berlin.
3. Bassoe, Peter: Epidemic Encephalitis, J. A. M. A. **72**:971 (April 5) 1919.

REPORT OF THE THIRD CASE

History.—A female child, 4 weeks old, vomited frequently for two days, and then repeated attacks of contractions of the diaphragm set in. When admitted to the Presbyterian Hospital, March 14, 1919, she was stuporous, with temperature ranging from 98 to 102 F. and a leukocyte count of 9,950. A laparotomy was performed and appendicostomy made. The following day the temperature rose to 103.2 F. and subsequently generally ranged between 100 and 102. A few days later nystagmus and strabismus were observed. The child died on March 25.

Necropsy.—This was held by Dr. B. O. Raulston and the following anatomic diagnosis was made: moderate hyperemia and edema of the brain; hyperemia of lungs; distention of urinary bladder; bilateral hydronephrosis; moderate dilatation of ureters; recent unhealed laparotomy wound; open stump of appendix; fatty changes in liver; patent ductus arteriosus and foramen ovale.

MACROSCOPIC EXAMINATION OF CASE 3

Macroscopically, the brain appeared practically normal. The pia was somewhat opaque, especially around the cerebellum; it was congested, rusty looking, but easily detachable from the brain substance. The convolutions were flattened, the sulci not gaping, the ventricles slightly dilated, the gray matter distinct from the white substance. There were no hemorrhages, no signs of ependymal changes.

MICROSCOPIC EXAMINATION OF THE THREE CASES

The brains from these three cases and the spinal cord of the third case were delivered to the laboratory fixed in a 10 per cent. formalin solution. Portions from every region of the hemispheres and brain stem, as well as from the spinal cord, were placed in 96 per cent. alcohol (for celloidin sections); some were prepared for paraffin, and a great number of frozen sections were also made from almost every portion of the central nervous system. The sections were stained by various methods, such as Mallory-Jacob, Alzheimer-Mann, Herxheimer (scarlet red), Bielschowsky, Weigert's elastic stain, toluidin blue, thionin, hematoxylin-eosin and many others.

The pia appeared infiltrated and frequently showed distended meshes containing congested, hyperemic vessels. The infiltration cells were mainly lymphocytes and plasma cells, about equally represented and especially numerous around the vessels. Numerous scattered cells were also seen in the meshes of the pial connective tissues (Fig. 1). Both the lymphocytes and the plasma cells appeared very densely stained, the latter showing a distinct cytoplasm and an excentrically located nucleus which exhibited the typical wheel-like arrangement of its chromatin and a distinct membrane. In contrast to these cells, the lymphocytes were represented by darkly stained, often homogeneous, nuclei, without any traces of cytoplasm. The latter was also absent in

many plasma cells which on superficial examination resembled lymphocytes. The plasma cells were not always of a typical appearance, but they were very numerous. Besides the lymphocytes and plasma cells, there were other forms present, but much less numerous, namely, fibroblasts, polyblasts, macrophages and rod cells — *Stäbchenzellen* (Fig. 2). The fibroblasts usually appeared as large, oval or round nuclei, filled with numerous small particles of chromatin, surrounded

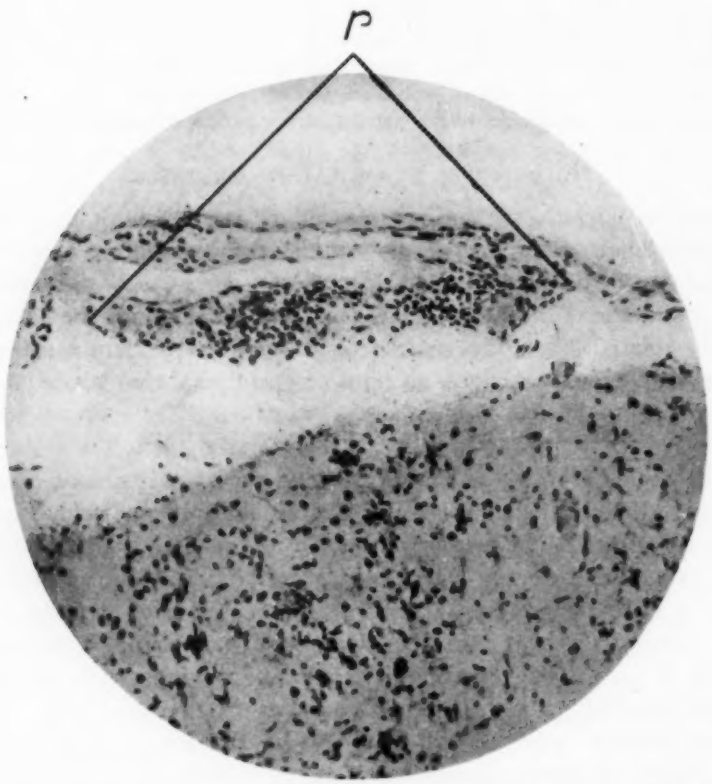

Fig. 1.—Infiltration of pia and cerebellar cortex. *P*, pia infiltrated and separated from the cerebellum. The molecular layer of the latter is much infiltrated by various cells as explained in the text. (Toluidin blue stain, × 150.)

by a well-formed membrane, but without any visible cytoplasm. They could easily be distinguished from the plasma cells and lymphocytes by their larger size and pale nuclei. Still fewer in number were certain other cells also with pale, irregular, often horseshoe-shaped nuclei, enclosed within a pale cytoplasm. These cells—polyblasts—were scattered singly or mixed with the three forms mentioned above.

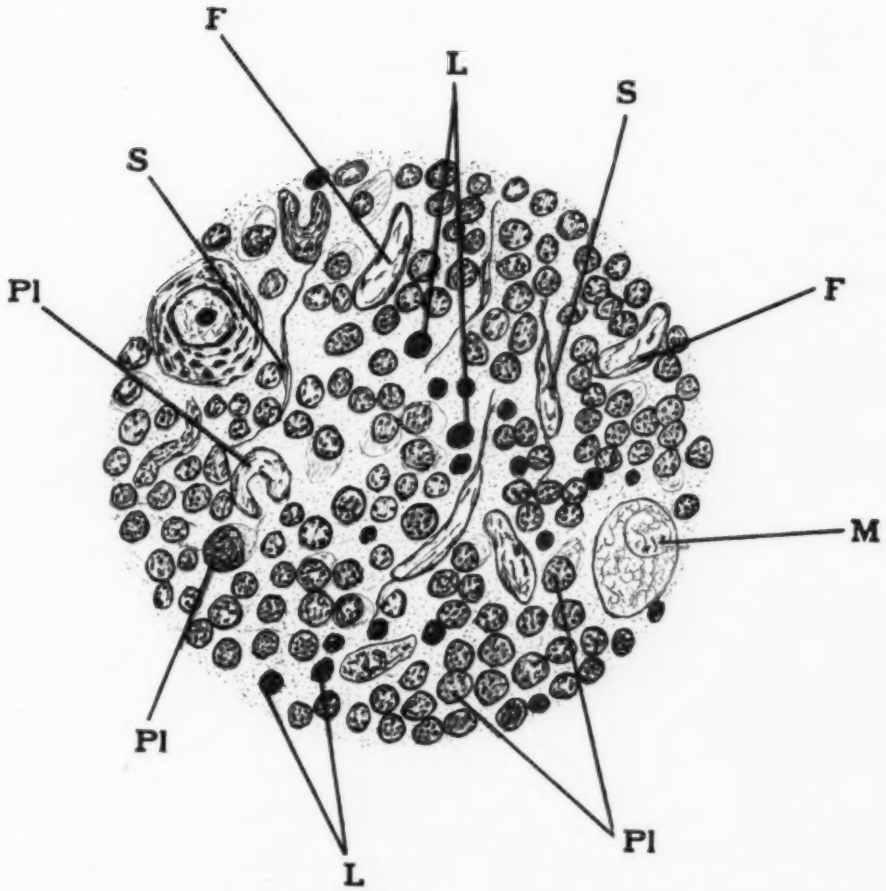

Fig. 2.—Types of various infiltration cells: L, lymphocytes; Pl, plasma cells; M, macrophage; Pb, polyblast; F, fibroblasts; S, *Stabchenzellen*. Toluidin-blue stain.

The macrophages were exceedingly rare, often contained small particles of blood pigment, or distinct vacuoles, and an excentrically located nucleus. The macrophages were seen only in those places where blood pigment was present, mostly as very minute particles.

Toluidin-blue specimens frequently revealed a great number of rod cells (*Stäbchenzellen*) especially near the vessels. They exhibited an

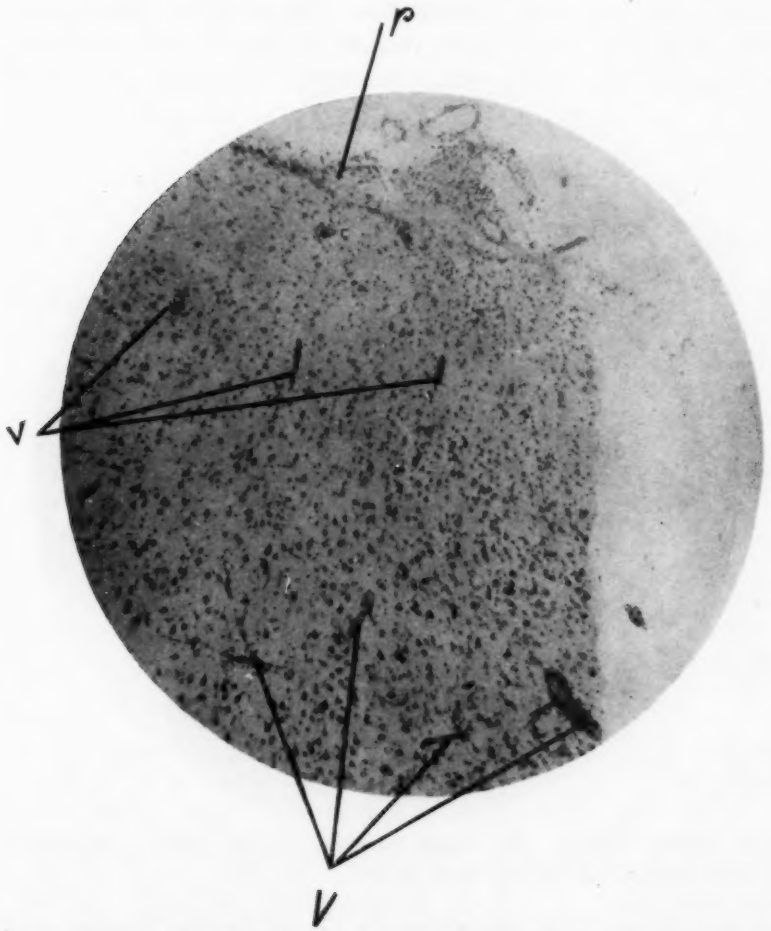

Fig. 3.—Cortex from the Island of Reil; the vascular infiltration especially in the deeper strata is very marked; the pia (*P*) is also infiltrated, but slightly. *V*, vessels. (Toluidin-blue stain, × 50.)

oblong, distinctly stained nucleus, with chromatin dots, and very pale cytoplasmic processes, emanating from the opposite poles. Any other cellular elements, such as mast cells, gitter cells and polymorphonuclear cells were not found. The infiltration was in evidence all over the pia, that is, around every part of the brain, but was especially marked

around the cerebellum, more so at the base, and it frequently involved the adjacent parenchyma. Figure 1 distinctly shows the invasion by the infiltration cells of the molecular layer of the cerebellum.

CLINICAL SIGNIFICANCE OF THE CHANGES OBSERVED

The pial changes, as outlined, indicate a mild leptomeningitis, more marked in some portions than in others, but not so pronounced as in paralytic dementia or in poliomyelitis. However, the pial changes in their character and localization, though less intense, very much resemble those described and pictured by Mott,[4] Spielmeyer and others[5] in

Fig. 4.—Pial vessels. The elastic membrane in the form of solid rings is very clear. (Resorcin-fuchsin stain, × 60.)

4. Mott, F. W.: The Changes in the Central Nervous Systems of Two Cases of Negro Lethargy, Brit. M. J. **2**:1666, 1889. The Cerebrospinal Fluid in Relation to Diseases of the Nervous System, Brit. M. J. **2**: (Dec. 10) 1904. The Examination of the Tissues of a Case of Sleeping Sickness in a European, Brit. M. J. **1**: 1904. Histologic Observations on the Changes in the Nervous System in Trypanosome Infections, Especially Sleeping Sickness, etc., Arch. Neurol. **3**:581, 1907.

5. Franca and Athias: Les Plasmazellen dans les vaissaux de l'écorce cérébrale, dans la paralysie générale et la maladies du sommeil, Compt. rend. soc. de biol. **54**:192, 1902. Spielmeyer, W.: Die Trypanosomenkrankheiten, Jena, 1908; also, Schlafkrankheit und Progressive Paralyse, München. med. Wchnschr. **54**:1065, 1907.

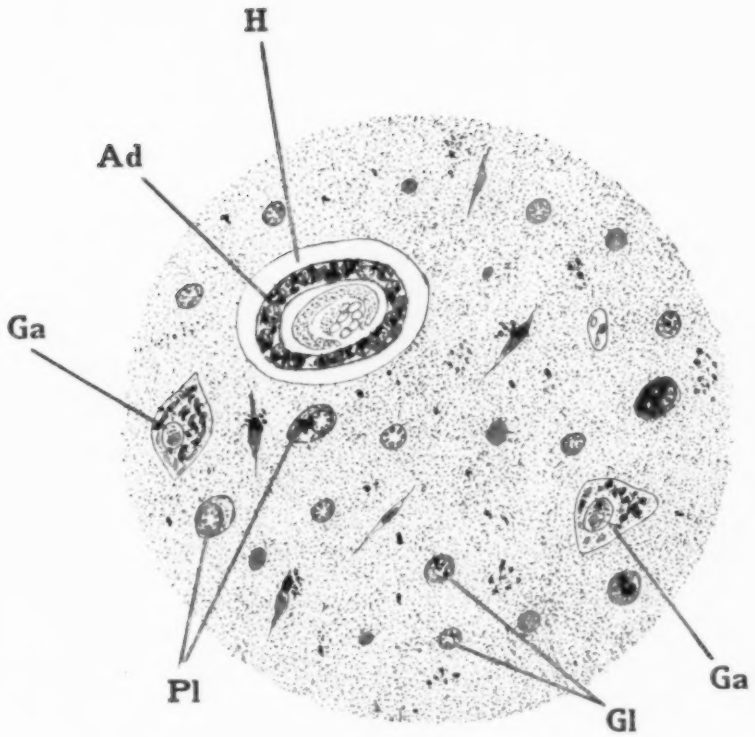

Fig. 5.—Substantia nigra. The ganglion cells, the glia nuclei, the adventitial space show fat globules which are also scattered all over the glia network in the form of minute droplets (Hematoxylin and Scarlet-red stain of Herxheimer.) *Gl*, glia nuclei; *Pl*, plasma cells; *Ga*, ganglion cells; *H*, His' space (Nissl's *Schrumpfraum*); *Ad*, adventitial space of Virchow-Robin.

trypanosomiasis. Vascular changes are much less constant and much less pronounced in the cortex of the cerebrum and the cerebellum. Dozens of sections may not show a single markedly infiltrated vessel. The few cortical perivascular infiltrations seen are small and, like the pial ones, more numerous in the cerebellum. Nevertheless, the cerebral cortex shows an abundance of other pathologic changes. The architecture of the various cell layers is practically unaltered, though some regions such as the occipital lobe, do not appear as richly supplied with ganglion cells as normally.

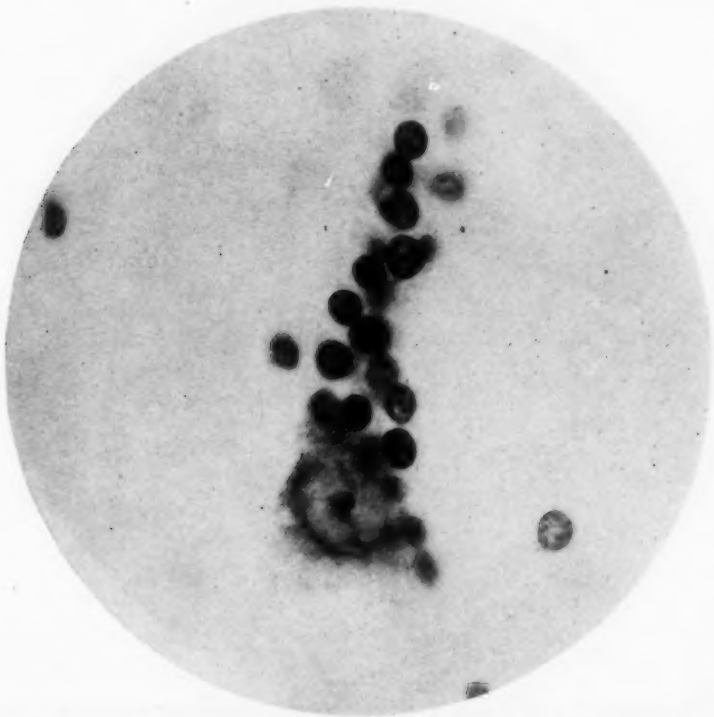

Fig. 6.—Type of neurophagia in the cortical and subcortical regions. The apical process as well as the right basal one are denesly covered by glia cells. The apical process is still visible beneath the glia cells. The cell body is very pale, the chromatin accumulated as a perinuclear cap. The round, free bodies scattered over the picture are also glia cells. (Toluidin blue stain, × 100.)

CHANGES IN THE CORTICAL LAYERS

As a rule, the cortical layers contain a great number of glia cells, mostly in the form of so-called glia nuclei, as well as an abundance of capillaries. Some sections exhibit a rich capillary network, the vessels appearing much congested, but without any signs of sprouting, endothelial proliferation or perivascular infiltration. Their intima shows a

well-stained endothelium, a free lumen not obscured or narrowed by a proliferated intima. The elastic membrane is homeogeneous, not split, powerfully developed and solidly blended with the intima. All these features are seen in Figure 4, which is taken from the pia whose vessels are identical in appearance with those of the brain. Many capillaries, in Herxheimer (scarlet red) specimens, show minute and larger drops of fat enclosed within the adventitial cells, in some instances forming a solid ring around the lumen (Fig. 5).

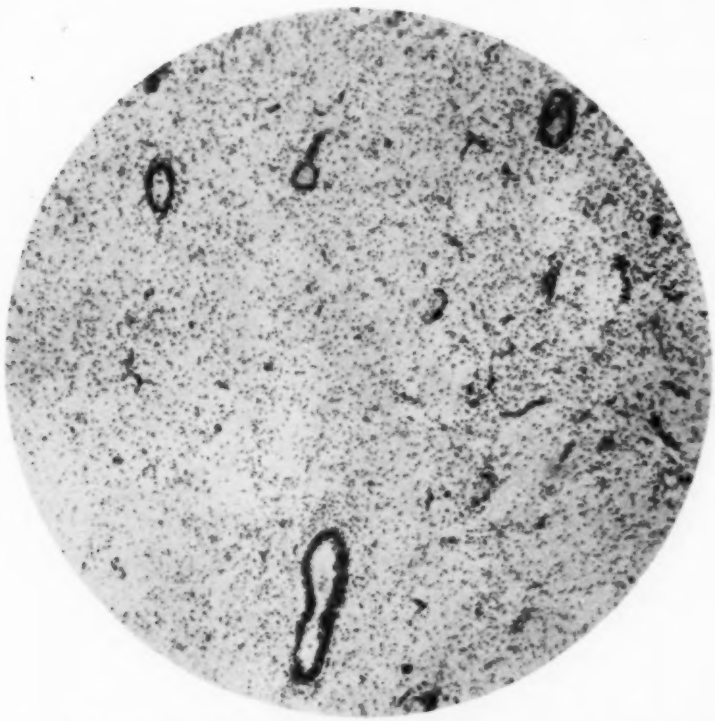

Fig. 7.—Infiltration of the optic thalamus, with numerous elements, explained in text. As compared with Fig. 5 the thalamus seems to be even more affected than the substantia nigra. (Toluidin blue stain, × 60.)

Generally speaking, the cortical mesodermal elements show few pathologic changes. These are, however, quite pronounced in the ectodermal elements, namely, the glia and the ganglion cells. Some of the latter are of normal size and structure, but the majority appear rather homogeneous, uniformly stained, without Nissl bodies, and with a dark, pyknotic or very pale, granular nucleus. In some cells the disintegration goes so far that only the nucleolus is visible. The cell processes are mostly densely stained, homogeneous, tortuous and without any traces of Nissl substance. All types of cell changes described by

Nissl are encountered, from the milder types, so-called chromatolysis and acute cell disease type, to the severe type when the cell body, including the nucleus, is reduced to an amorphous, granular mass invaded by glia cells—"neuronophages" (Fig. 6). Other less damaged cells are merely thickly surrounded by them (satellitosis). Satellitosis, chromatolysis and neuronophagia are the most common alterations to be met with in the cortex, especially in the deeper strata. In scarlet red specimens many cells, especially in the deeper layers, show droplets of fat

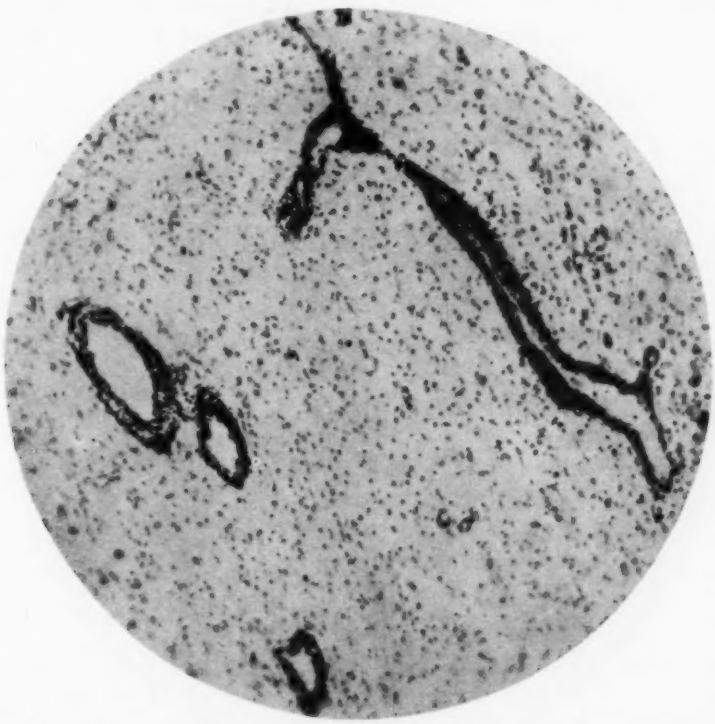

Fig. 8.—Substantia nigra is covered by densely infiltrated vessels and numerous glia nuclei, especially to the right of the larger vessel. Some of the dots are free plasma cells and other bodies, as explained in text. (Toluidin-blue stain, × 110.)

mostly at the base of the cell, often surrounding the nucleus in the shape of a semicircle. The glia tissue, as we said, shows a marked proliferation of its cells, some of which have abundant protoplasm, but the majority are in the form of large nuclei rich in chromatin (Fig. 5). Astrocytes are absent, and glia fiber proliferation, as well as regressive changes, like ameboid glia, "fill bodies" (*Füllkörperchen* of Alzheimer), various granula and glia reticulum are totally lacking.

These parenchymatous changes are much more marked in the subcortical regions, the basal ganglia, subthalamic area and tegmentum. In these regions they are not only very pronounced, but they are also combined with profound interstitial changes. Thus, the vascular infiltrations are enormous (Figs. 7, 8, 9), in the case of some smaller arteries compressing their lumina, giving them the shape of a figure 8, or in the case of capillaries and small veins totally obscuring their shape (Fig. 9). The infiltration elements—lymphocytes, plasma cells, poly-

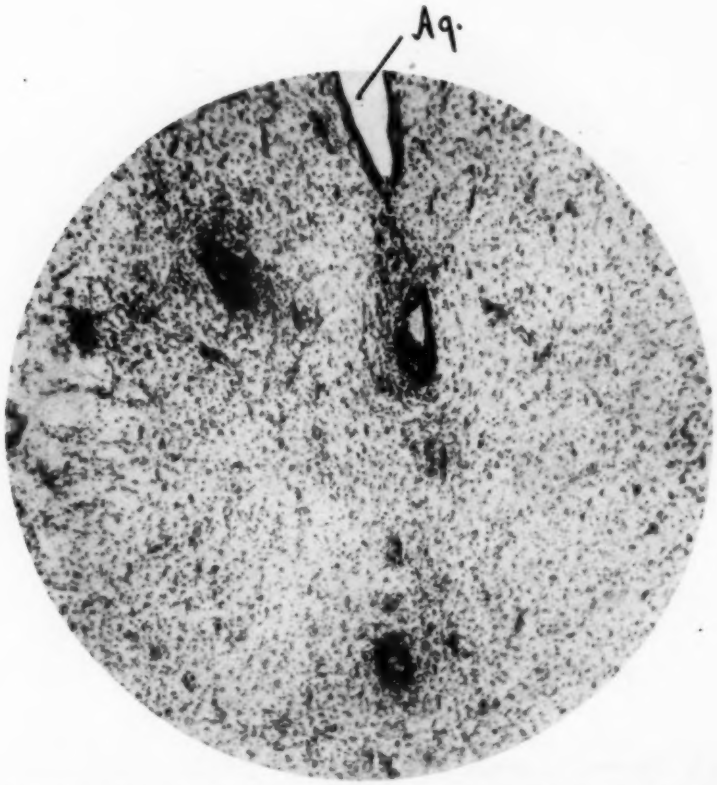

Fig. 9.—Tegmentum of pons. Infiltration of the vessels and of the formatio reticularis. *Aq*, Aqueducts Sylvii covered with ependyma cells. (Toluidin-blue stain, × 65.)

blasts, fibroblasts, rod cells—are principally confined to the adventitial spaces of Virchow-Robin, but sometimes they are so dense that these spaces seem to be overflowed by the cells, and an impression is gained that the space outside the adventitia, between the latter and the brain—the so-called perivascular space of His—is also invaded. Careful observation, however, shows that the latter is usually free, and that the infiltration is exclusively confined to the Virchow-Robin spaces as well as

to the distended meshes of the adventitia. In some places, like the optic thalamus and substantia nigra, the infiltration cells can be seen invading the parenchyma itself (Figs. 10, 11, 12), yet it is sometimes difficult to make out whether the invading elements (plasma cells and rod cells) traveled from a densely infiltrated vessel or are merely the focal products of inflamed or infiltrated minute capillaries.

CELLULAR ELEMENTS FREELY PRESENT

At any rate, some parts like the optic thalamus and substantia nigra, show a wealth of various cellular elements, including glia cells, all mixed in irregular masses, which surround vessels, capillaries and

Fig. 10.—Typical plasma cells *(P)* along a dendrite of a deeply changed ganglion cell. (Toluidin-blue stain, × 1,200.)

ganglion cells. Many vessels, especially the smaller ones, are not only densely infiltrated, but also congested, packed with blood pigment, some containing hyaline and other thrombi (Fig. 13). In spite of such marked infiltrative phenomena, some ganglion cells—especially in the substantia nigra — appear quite normal, though the majority show various changes (chromatolysis, neuronophagia and even cell sclerosis). As in the pia and cortex, hemorrhagic foci, gitter cells, foci of softening and polymorphonuclear cells are totally lacking. Only very minute capillary hemorrhages were found, and once a larger hemorrhage could be seen surrounding a congested small vein. In both instances, however, reactive phenomena in the neighborhood of the hemorrhagic foci

were absent, and it is probable that these hemorrhages were terminal or agonal. In this connection, we should mention numerous red bodies—spherules—throughout the spinal cord of Case 3, in the gray as well as the white matter (Fig. 14). They are round and regular in shape, lying singly in the parenchyma or near the capillaries and even in the perivascular, adventitial spaces. They are smaller than red cells, are much more densely stained with eosin, are perfectly homogeneous and not enveloped by glia tissue. The latter is not thickened or proliferated around them. It is hard to tell at the first glance whether these bodies are plain erythrocytes, or formations described as cystic plasma cells (cysto-plasmatozyta) by Perusini[6] and also depicted by Favorsky[7] in

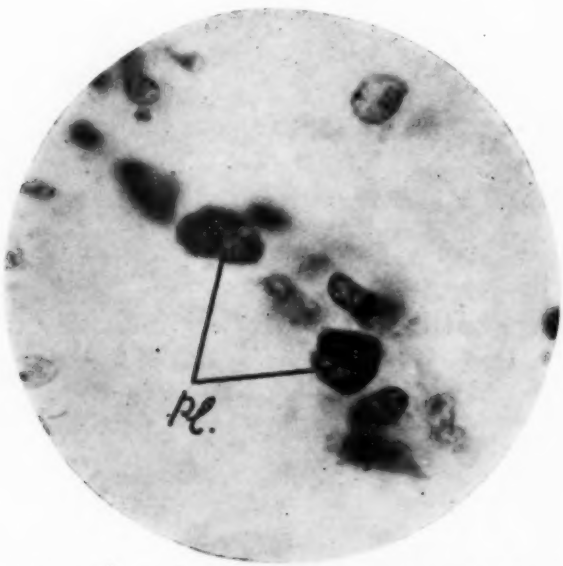

Fig. 11.—A degenerated ganglion cell (from substantia nigra) *invaded* and surrounded by plasma cells (*Pl*). (Toluidin-blue stain, × 1,200.)

a case of tabes dorsalis. Still more do they resemble the bodies described by Fulci,[1] so it would appear proper to call them the *spherules of Fulci.* They show very well in Alzheimer-Mann specimens, appear in Bielschowsky specimens as round, pale brown bodies, and do not show at all with thionin, toluidin blue, hematoxylin-eosin or scarlet red stains, while in the brain tissue they cannot be demonstrated at all.

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6. Perusini, G.: Sopra Speciali Cellule Degli Infiltrati Nel Systema Nervoso Centrale, Riv. sper. di Freniat. **36**:721, 1910.

7. Favorsky, A.: Die Abbauerscheinungen bei Tabes Dorsalis, Nissl-Alzheimer's Arbeiten, **6**:74, 1913.

NO DEGENERATION PROCESSES OBSERVED IN SUBCORTICAL FIBERS

In spite of the marked ganglionic and interstitial changes, no degeneration of the subcortical fibers is found, nor are there any myelophages, gitter cells or other evidence of secondary glia changes. As in the cortex, the glia changes in the subcortical areas are of a progressive nature, represented by glia cells rich in protoplasm, or large-sized glia nuclei rich in chromatin. In the spinal cord there are, in addition, a great many astrocytes. The pons, medulla and spinal cord show the same intensity of interstitial changes as the large ganglia and midbrain. The spinal canal is usually occluded, either by proliferated ependyma

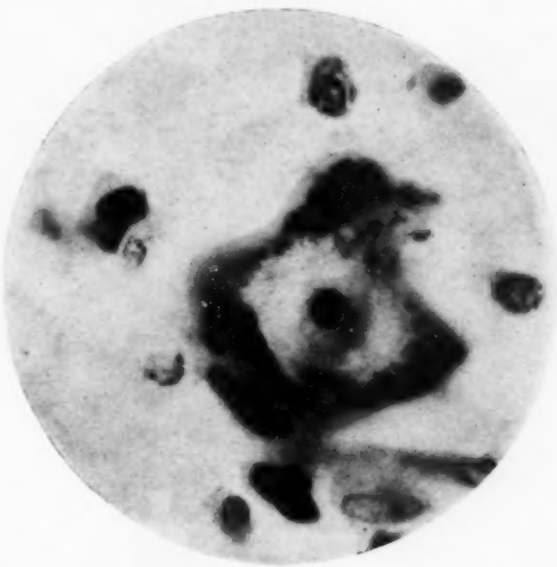

Fig. 12.—A destroyed ganglion cell from the subthalamic region surrounded by plasma cells. (Toluidin-blue stain, × 1,200.)

cells, or by an amorphous mass mixed with lymphocytes and certain thin, elongated bodies stained dark with Bielschowsky's method (probably bacilli).

SUMMARY OF HISTOLOGIC STUDY

In summing up our histologic findings we may say that they concern the mesodermic (interstitial) and ectodermic (parenchymatous) elements. In the cortex, the parenchymatous changes predominate; in other regions (peduncles, internal capsule, lower portion of pons, bulb and cord) the interstitial changes predominate, while in the basal ganglia, substantia nigra and tegmental region of pons, both types are equally in evidence. In other words, the parenchymatous and inter-

stitial changes may exist independently of each other, and an absolute relationship between them cannot be claimed.

Both these large groups of pathologic changes are, according to Nissl and his school,[8] essential in and characteristic of an encephalitis. It is needless to state that the above-described findings would satisfy

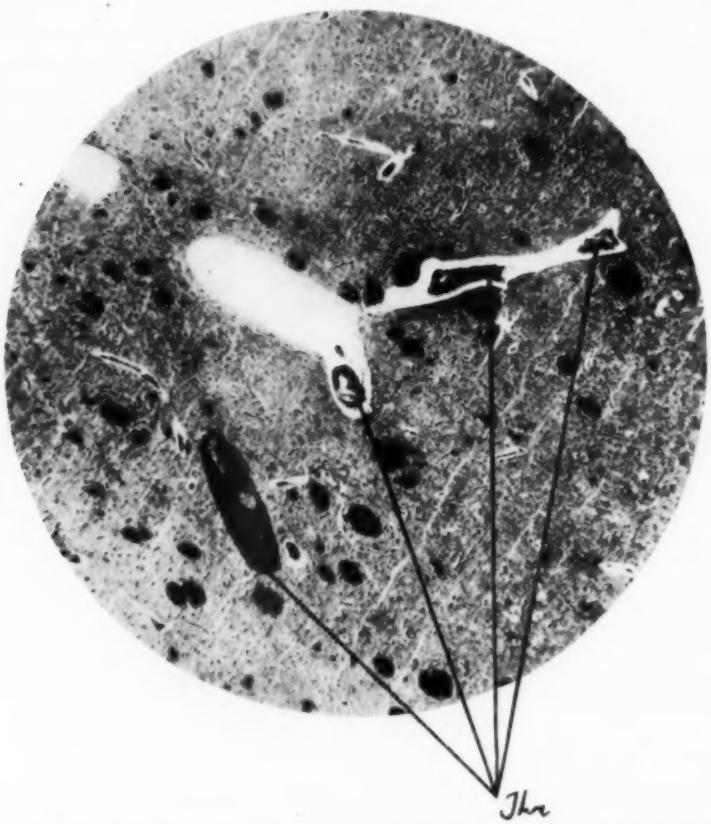

Fig. 13.—Nucleus candatus (its head bordering on the lateral ventricle). The numerous light channels inclosing vessels are so-called *Schrumpfräume* of Nissl; the large black spots are bundles of white cortical fibers *(Haubenfasern)* of the cortex; the small dots are glia nuclei. Some vessels show so-called hyaline thrombi (*Thr*). (Bielschowsky stain, × 50.)

even such a severe critic as Nissl that our three cases are instances of an encephalitis, resembling as they do in their pathologic features paralytic dementia, sleeping sickness and poliomyelitis.

By the absence of foci of softening, of large hemorrhages, of gitter cells, of polymorphonuclear elements, the lethargic form of encephali-

8. Ranke, Otto: Beiträge zu der Lehre von Meningitis Tuberculosa, Nissl-Alzheimer's Arbeiten **2**: 1908.

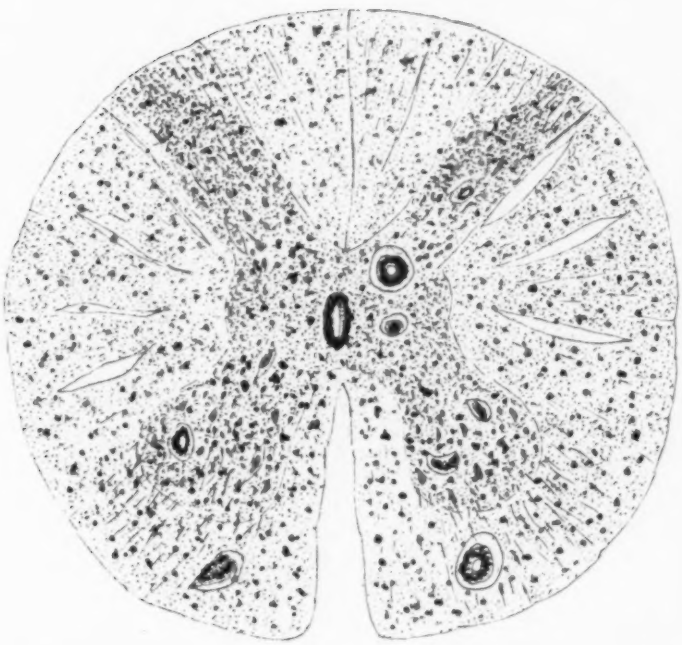

Fig. 14.—Spinal cord from Case 3 (lumbar region). The ependyma of the central canal, the blood vessels, the gray and white substances show an abundance of red spherules described in the text. (Frozen section; Alzheimer-Mann stain.)

tis, in our own cases at least, differs from other types, like Wernicke's polioencephalitis superior hemorrhagica,[2] acute hemorrhagic encephalitis,[9] influenzal encephalitis,[10] traumatic and experimental encephalitis (Friedman,[11] Coen,[12] Lottmar[13] and many others). In Wernicke's

Fig. 15.—Lumbosacral portion of the spinal cord (Case 3). The membranes are slightly infiltrated; the subarachnoid space shows on the left a congested vein; the anterior and posterior horns exhibit a number of infiltrated vessels; the number of ganglion cells in the anterior horns is normal; the ependyma cells of the central canal are proliferated (a magnifying hand-glass will show the details better). (Toluidin-blue stain, × 16.)

9. Deiters: Ueber Haemorrhagische Encephalitis, Neurol. Centralbl. **17**: 722, 1898. Friedman: Deutsch. Ztschr. f. Nervenh. **16**:93, 1899. Brie: Neurol. Centralbl. **16**:2, 1897. Schmidt: Deutsch. med. Wchnschr. **18**:703, 1892. Sträussler: Jahrb. f. Psych. u. Neurol. **21**:253, 1902.

10. Bücklers: Arch. f. Psych. **24**:730, 1892. Königsdorf: Ein neuer Fall von acuter Haemorrhagischer Encephalitis waehrend der jetzigen Influenza-Epidemie, Deutsch. med. Wchnschr., 1892, p. 182. Fürbringer: Deutsch. med. Wchnschr. **18**:182, 1892. Oppenheim, H.: Deutsch. Ztschr. f. Nervenh. **6**:398. Oppenheim and Cassirer: Encephalitis in Nothnagel's Encyclop. **11**:2, 1907.

11. Friedman, M.: Studien zur Pathologischen Anatomie der acuten Encephalitis, Arch. f. Psych. **21**:461, 1890; also, Neurol. Centralbl. **8**:441, 1889.

12. Coen, E.: Ziegler's Beiträge zur Pathologischen Anatomie, etc. **2**:107, 1888.

13. Lottmar, Fritz: Beiträge zur Histologie der akuten Myelitis und Encephalitis, sowie verwandter Prozesse, Nissl-Alzheimer's Arb. **6**:248, 1913.

form and the so-called hemorrhagic encephalitis the hemorrhages are the principal feature with abundance of reactive phenomena on the part of the glia and total lack of parenchymatous, ganglionic changes. In fact, the characteristic signs of encephalitis, as outlined above, are absent in these two forms, which fact has been already pointed out by Biet,[14] Redlich[15] and Schroeder.[16] These authors justly doubt whether Wernicke's polioencephalitis should be called encephalitis at all. The same can be claimed for the influenzal and other forms in which practically the only lesions are hemorrhages. In the traumatic and experimental forms, foci of softening or necrobiosis are common, which are, however, totally foreign to the lethargic type.

COMMENT

Our histologic studies thus have brought out the fact that the epidemic encephalitis distinctly differs from the condition previously described as influenzal encephalitis. Hence, if the influenzal encephalitis of previous authors really is influenzal, the form now under discussion decidedly is not. As stated before, it resembles the African sleeping sickness, dementia paralytica and the acute anterior poliomyelitis. The resemblance to the sleeping sickness is so great that a differential diagnosis on histologic basis is impossible. However, the sleeping sickness is chronic or subacute, while the lethargic encephalitis is rather acute in its course. The infiltrations of the pia and cortex are more pronounced in sleeping sickness. The slight difference in some pathologic changes (for instance, an occasional proliferation of vessels) may be explained by the longer duration of the African disease. It is also difficult to differentiate the brain changes of epidemic encephalitis from those of paralytic dementia. In the latter, however, the meningeal infiltration is very pronounced; the infiltration cells are mostly plasma cells, there is marked new formation of capillaries, a distinct proliferation of the intimal layer and of elastic fibers is present; all these changes being *especially pronounced in the cortex*.

As some of these characteristic features, like intima and elastica changes and proliferation of vessels, may be absent in acute cases of dementia paralytica and sometimes may be even more pronounced in the subcortical regions (the atypical forms of Lissauer and Alzheimer), it is clear that it may sometimes be difficult to differentiate these two diseases.

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14. Biet: Contrib. a l'étude des affections nerveuses consecutives à la grippe, Paris, 1895. (Quoted from Friedmann, Footnote 9.)

15. Redlich, E.: Ueber Encephalitis Acuta, Centralbl. f. Allg. Path. **11**:513, 1900.

16. Schröder, Paul: Zur Lehre von der Akuten Haemorrhagischen Polioencephalitis Superior (Wernicke), Nissl's Arb. **2**:145, 1908.

In poliomyelitis the changes are largely confined to the spinal cord, the cerebral forms being very rare. Suffice it to say, that the spinal cord changes of Case 3, though much resembling those of acute poliomyelitis (vascular infiltration), are by no means identical with them. Hemorrhages, foci of softening, polymorphonuclear cells, marked satellitosis, so frequent and common in acute anterior poliomyelitis, are missing, while the parenchymatous and meningeal changes usually so marked in poliomyelitis are not striking in our case (Fig. 15).

The brief analysis of our findings shows a similarity in all essential points to those described in epidemic encephalitis by Marie,[17] Marinesco[18] and others.

CONCLUSIONS

1. The pathologic changes in epidemic (lethargic) encephalitis involve the entire central nervous system.

2. These changes are both parenchymatous and interstitial.

3. The former principally involve the cortex, the latter the peduncles, internal capsule, lower pons, bulb and cord. In the basal ganglia and midbrain both parenchymatous and interstitial changes are pronounced.

4. In its histopathology epidemic (lethargic) encephalitis differs from the various types of hemorrhagic encephalitis, but it is identical with that of African sleeping sickness (trypanosomiasis).

5. It differs from typical cases of paralytic dementia by the topography of the lesions and by absence of vascular wall changes, which probably are due to the more chronic course of the latter.

6. It also differs from the various types of traumatic and experimental encephalitis and from acute anterior poliomyelitis.

7. It is pathologically a distinct morbid entity, a disease *sui generis*, and does not resemble the conditions previously described as influenzal encephalitis.

8. The similarity between the pathologic changes in African sleeping sickness and epidemic encephalitis suggests a close relationship of their etiologic factors, that is, the epidemic encephalitis may be caused by a parasite akin to a trypanosome.

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17. Marie, Pierre and Tretiakoff, C.: Examen histologique des centres nerveux dans deux cas d'encephalite lethargique, Bull. et mem. Soc. med. des hôp. de Par., May 24, 1918.

18. Marinesco, G.: Contribution a l'etude de l'histologie pathologique de l'encephalite léthargique, Bull. de l'Acad. de méd. **80**:411, 1918.

DISCUSSION

DR. MAX H. WEINBURG, Pittsburgh: Speaking of the difference between what Dr. Bassoe found and the findings of the other workers such as Welsh and Marinesco regarding the differentiation of poliomyelitis and lethargic encephalitis, the findings are not in accord with those of the other workers. Marinesco pointed out that there are more plasma cells in the latter condition, and Welsh corroborated him. Marinesco pointed out that there is no neuronophagia or very little. This disease is of such wide manifestation that you will find a different pathology in the cases, just as clinically such cases manifest symptoms altogether different. There are many punctate hemorrhages found all over the brain. In one case we had in New York the lesion was believed to be a tumor. Most of the neurologists believed it to be a sarcoma of the brain. At necropsy a large hemorrhage can be explained readily by the fact that the disease in some cases is more marked than in others, and therefore there is some variance in results. Welsh reported several cases of the cord where there were cervical lesions, but in one case the lesion was as far down as the lumbar region. Clelland of Australia who has experimented on 120 animals points out mainly the perivascular infiltration and that the disease can be transmitted. The differential points between poliomyelitis and encephalitis lethargica are that there is no or little neuronophagia as there is in poliomyelitis, the plasma cells predominate, and there is little parenchymatous change, and it is for that reason that most of these patients recover. There is a prevailing belief that this is a disease of high mortality, but this is merely due to the fact that a great many cases are not recognized. I have had occasion to see over sixty cases in New York with a very low mortality.

DR. PETER BASSOE, Chicago: In regard to the question of cell changes, I can only relate my own experience. At the time I reported my first two cases I stated that hemorrhage was marked and there were no cell changes. After making a thousand checks we found the hemorrhage was an accidental finding. I happened to strike the only hemorrhage the first time. You must make sections all through and conduct your investigation with an open mind. I find hemorrhages are not a feature and neuronophagia is. It is, to be sure, not overly profound. You can look at a dozen sections, particularly of the cortex, without finding it, but deeper down you will not miss it. I have now a brain from a patient who had an acute encephalitis, and there is an extensive condition throughout the brain. It may be a true influenzal encephalitis. I am not prepared to say anything about the relation of this disease and influenza; only if what has previously been described is influenzal encephalitis, then this is not. As to the Australian cases, we have to be a little slow, as we do not know what they were. Many of the reports look like poliomyelitis, and one of the foremost investigators there believes the cases were poliomyelitis.

GENERAL PARALYSIS TREATED BY INTRAVENTRICULAR INJECTION OF ARSPHENAMIN

REPORT OF THE NECROPSY FINDINGS IN A CASE *

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Following the discovery of the *Treponema pallidum* in the brain in cases of general paralysis, and encouraged by the reported favorable results obtained in the treatment of neurosyphilis by the intraspinal injection of arsphenamin as advocated by Swift and Ellis and by Ogilvie, many men began to treat general paralysis with arsphenamin, administering the drug either by the intravenous or intraspinal method. The results obtained are now well known to those who have followed the evolution of therapy of neurosyphilis since the introduction of arsphenamin. Failing to obtain as favorable results from the use of arsphenamin in paresis as from its employment in the more benign forms of neurosyphilis, and stimulated by the results from animal experimentation, Hammond and Sharpe[1] introduced a method of injecting arsphenamin into the ventricles of the brains of the cases of general paralysis, hoping to get the drug more closely to the site of the pathologic process. They reported a series of cases which showed clinical improvement following this mode of treatment. Many observers were impressed with these results, and Neymann and Brush,[2] in their analysis of the different forms of treatment of paresis, spoke very favorably of this method.

The following case is of interest as it is the first case which has received this form of therapy, and has been studied clinically as well as at the postmortem examination.

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* From the Department of Pathology, Manhattan State Hospital, Ward's Island, N. Y.

* Presented before the New York Neurological Society, Oct. 1, 1918.

1. Hammond, G. M., and Sharpe, Norman: The Treatment of Paresis by Injections of Neosalvarsan into the Lateral Ventricle, J. A. M. A. **65**:2147 (Dec. 18) 1915.

2. Neymann, C. A., and Brush, N. H.: The Treatment of General Paresis, Arch. Int. Med. **22**:245 (August) 1918.

REPORT OF CASE

History.—H. F., a man aged 40, was born in New York City of German parentage. He was graduated from the public school. He married in 1905 and has one living child; no miscarriages. He drank early in life, but he was a good provider for the family. He was of a happy disposition and was well liked by his friends. He has had several attacks of rheumatism. No knowledge of any venereal diseases. Worked satisfactorily as a carpenter. In December, 1915, he showed the first evidence of the disease, becoming forgetful. He continued to work until the middle of 1916, when his memory became so poor that he had to discontinue his work. At the same time he became irritable, showed speech defect, and began to manifest unsteadiness in walking. He later became grandiose in his statements, saying that he was a millionaire, etc. He finally became very restless and was sent to the Post-Graduate Hospital for treatment.

Clinical Course.—In March, 1917, he received one intraventricular injection of arsphenamin, through a trephined opening in the skull. Subsequently he was transferred to Bellevue Hospital, where he was characterized by the physicians as being simple, childish, dull in speech; wandered about in an aimless manner; was very irritable; was expansive in his statements; his pupils were small and irregular and did not react to light; knee jerks were increased.

Examination.—He was admitted to the Manhattan State Hospital on May 16, 1917. An examination in this institution revealed considerable mental deterioration; he said he was a carpenter and that he was feeling fine, and that he had to go to work. He did not know when he was married. He was disoriented. He had no memory on immediate past. He did small calculations very poorly. His speech showed considerable defect. He could not interpret what he had read. He had no insight. He expressed grandiose ideas. His judgment was poor. Physically, he showed good nutrition. Pupils were irregular, unequal and reacted very sluggishly to light. Spinal fluid showed positive globulin, 54 cells, and a ++++ Wassermann reaction.

Subsequent History.—He soon began to soil himself and became quite ataxic. He was very euphoric in the latter part of May, and his speech became so defective as to be hardly understood. On June 27 he developed convulsions and died on the following day.

ANATOMIC SUMMARY

Necropsy performed fifteen hours postmortem. The remains of a well developed, and of a moderately well preserved man appearing about 40 years of age. Rigor mortis was present in all extremities. Excepting slight abrasions over the sacrum and over the right knee, there was nothing of significance noticed in the skin of the body. Over the junction of the parietal and frontal bones, just to the left of the midline, a distinct depression of the scalp was seen. This was due to a defect in the subjacent bone evidently caused by a trephined area in the skull, 3 by 2 cm. in size. The scalp at this area was adherent to the subjacent dura. The calvarium stripped with considerable ease, and left a pale dura beneath it. Immediatelly beneath the trephined area in the skull there was a semicircular incision in the dura; the

resultant flap in the dura was half the size of a 5-cent piece. The edge of the flap was adherent to the subjacent pia-arachnoid by only very thin fibrous tissue, and it could readily be lifted from the underlying tissue. The dura as a whole appeared quite pale, and over the anterior

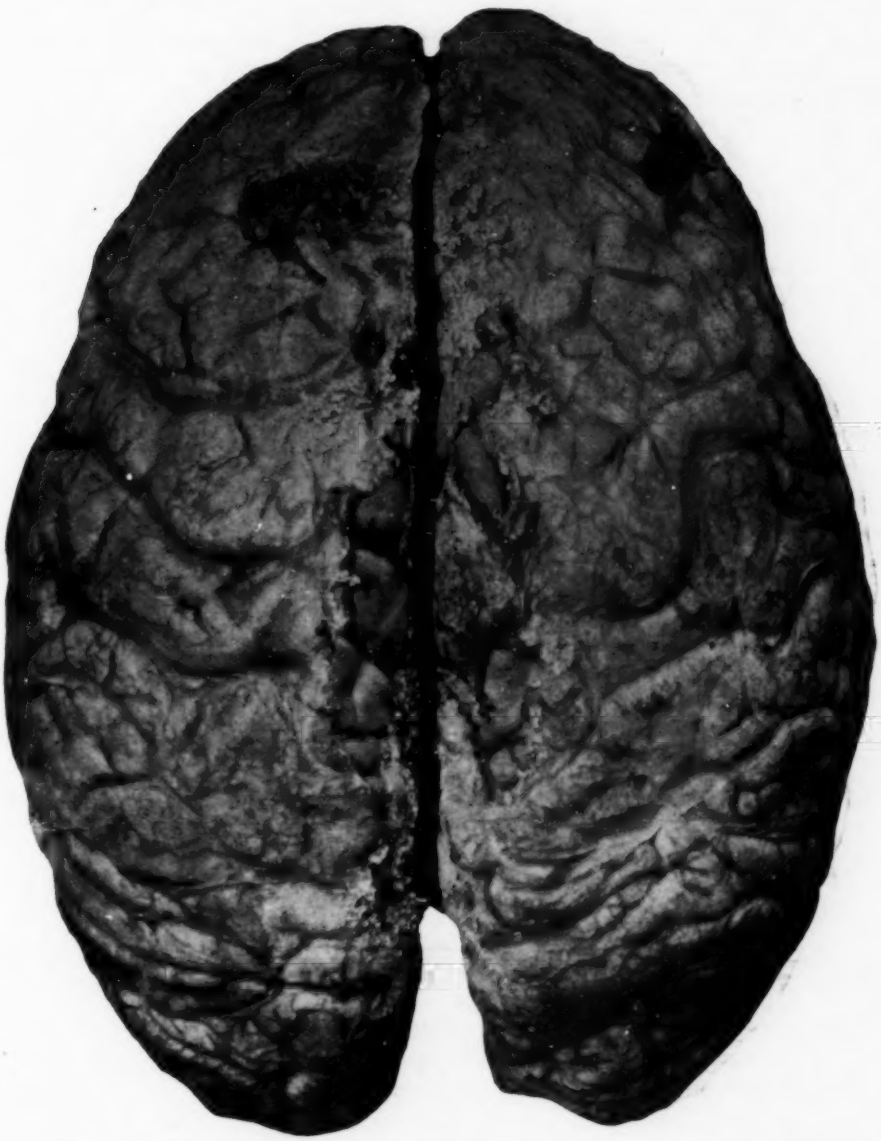

Fig. 1.—Note thickened pia and characteristic appearance of exudate. Left hemisphere more involved than right. The defect in the right frontal lobe was caused by removal of a section for fixation in alcohol. The pia-arachnoidal flap is in the plane of the arrow.

third of the brain, most marked over the frontal poles, it was decidedly puckered and redundant. There was no pathologic condition found in the dura. The vessels in the dura were of the normal size and

Fig. 2.—Note exudate on the base of the brain. Lesion is greater on the left side. Note exudate over the left side of the cerebellum. The defect in the right gyrus rectus was caused by removal of section for fixation in alcohol.

appearance. On incision of the dura and arachnoid an excessive amount of cerebrospinal fluid escaped.

The brain weighed 1,175 gm. It was of medium size, and its consistency was about normal. The pia over the anterior two-thirds of the brain showed a characteristic milky cloudiness and thickness; over the posterior third of the brain the pia was fairly clear and glistening. The base of the brain, especially over the interpeduncular spaces, showed thickened and clouded pia. The pia over the left hemisphere was decidedly more thickened and evidently more involved than the pia over the corresponding parts of the right hemisphere. The pia over the cerebellum, and also in the ponto-cerebellar angles, was of a milky, clouded appearance. On lifting the flap of dura immediately beneath the trephined area in the skull there appeared a part of the brain cortex, evidently due to the adhesion of the dural flap to the subjacent pia-arachnoid. Characteristic granulations were seen in the gyri recti and in the ventricles, especially on the floor of the fourth ventricle. There was considerable atrophy in the frontal lobes, the convolutions being well rounded out and the sulci and fissures were quite wide and shallow. The large vessels, namely, the basilars, internal carotids, and the cerebrals were quite normal in their macroscopic appearance. No hemorrhagic areas were noticed.

Sections from the superior frontal, precentral, paracentral and occipital convolutions, from the gyrus rectus, and from the lobule immediately beneath the trephined area, and from the medulla and cerebellum were examined microscopically. The pia showed considerable edema; there was present the characteristic lymphoid and plasma cell infiltration, especially about the pial vessels; numerous mast cells were also seen; the exudate was greater in the sections from the left hemisphere. The neuroglia layer was thicker than normal, and throughout the cortex there was noted an increase in neuroglia cells; in several places there were typical pictures of satellitosis. The cortex showed considerable disorganization; there was much edema; the cells were found in all stages of degeneration and characteristic pictures of cloudy swelling and granular degeneration were noticed, especially in the sections from the left hemisphere. The perivascular exudation of lymphoid and plasma cells was quite striking. Numerous mast cells and a small number of rod cells were also noted. The sections from the cerebellum and from the occipital lobule showed very slight pathologic changes as compared with the sections from the other regions studied. The sections from the left hemisphere showed more edema, greater exudation and a more advanced cortical disorganization than the sections from the right hemisphere. The spinal cord showed nothing of significance macroscopically; but microscopically,

considerable degeneration was noticed in the fibers of the posterior columns stained by the Marchi method. Sections from the right optic nerve showed many lymphoid and a few mast cells running through the nerve. The other cranial nerves showed no significant changes macroscopically. The internal ears were opened and found in normal condition.

Fig. 3.—Note infiltration of pia with lymphoid and plasma cells; considerable edema of pia is present. Note increase in neuroglia cells in the adjacent cortex.

The *pituitary* gland did not present anything of significance. The *thyroid* gland was of normal appearance; the alveoli were distended with colloid and the cells were definitely flattened. The *thorax* was externally symmetrical; the sternum stripped with ease; the costal cartilages were not calcified. Both pleural cavities were free from fluid, but each contained moderately dense adhesions in the apices.

The *right lung* weighed 580 gm. and the left 560 gm.; the apices showed definitely healed tuberculous nodules which had been partly replaced by calcium salts, and between these nodules there were numerous strands of connective tissue; the posterior portions of the lower lobes showed distinct edema and bronchopneumonic patches.

The *pericardium* was free from fluid and adhesions. The *heart* weighed 330 gm.; it was covered on its anterior surface by a very

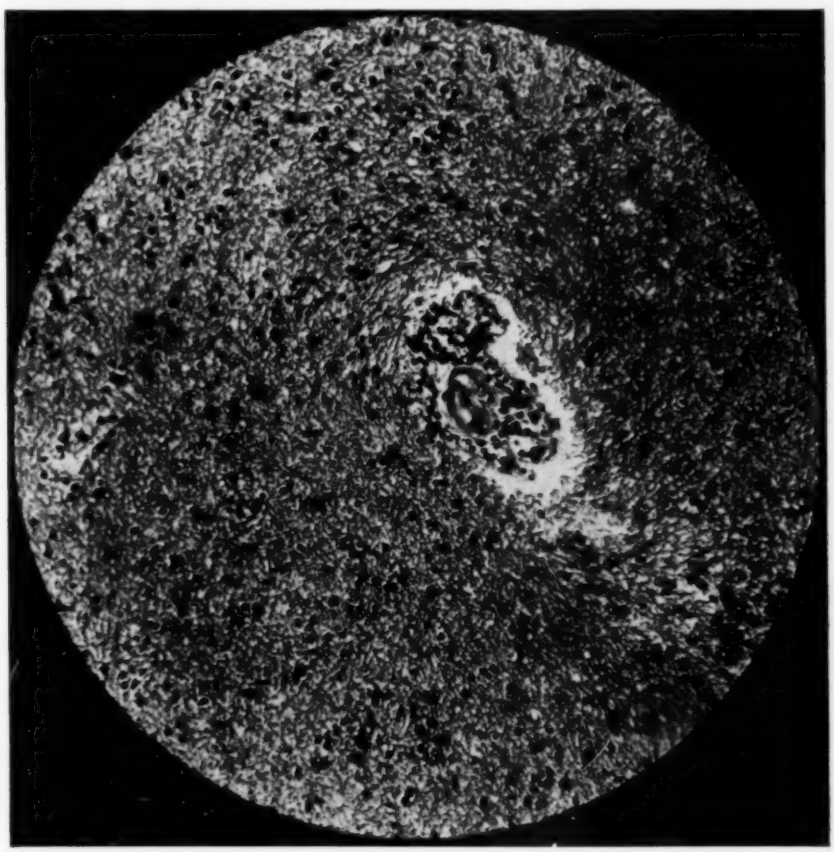

Fig. 4.—Note the perivascular exudation of lymphoid and plasma cells around two small cortical vessels. There is also seen an increase in neuroglia cells in the cortex.

thick fat pad; it was of normal size and consistency; all valves were compensating and their cusps were quite delicate; the papillary muscles were normal in appearance; the coronaries were patent. The *aorta* presented a characteristic picture; the arch was definitely dilated; there was a decided loss of elasticity in the entire aorta; throughout the thoracic portion there were numerous linear scars and pearly nodular

elevations; the abdominal portion was relatively free and only an occasional yellow-colored ulcerated area was seen; microscopically, the intima presented a fairly normal appearance; the media was infiltrated with many lymphoid and plasma cells which in places were grouped and assumed a picture which was highly suggestive of miliary gummas, the adventitial vessels showed perivascular exudations of lymphoid and plasma cells.

The *abdomen* was scaphoid; the panniculus adiposis was of medium size and of normal color; the peritoneal cavity was free from fluid; the omentum extended into the pelvis and in the left hypochondrium it was adherent to the peritoneum by thin but firm adhesions. The appendix was entangled in a mass of adhesions; it had an injected inflammatory appearance. The *stomach* was distended with gas and was otherwise of a normal appearance; the rest of the intestinal tract showed nothing of importance. The *spleen* weighed 130 gm.; it was of a normal size and appearance, and of a slightly increased consistency. The *liver* weighed 1,450 gm.; it was somewhat larger than normal, and its color was definitely yellow and its consistency was diminished; microscopically, the cells showed a condition of fatty infiltration and cloudy swelling. The gallbladder was distended with bile; all ducts were patent. The *pancreas* showed nothing remarkable. The *adrenals* were of normal size and consistency, and on section presented a normal cell layer arrangement.

The right *kidney* weighed 110 gm. and the left 140 gm.; the right appeared normal, but the left kidney showed a few adhesions between the capsule and the cortex, and the cut section presented a rather boiled appearance. The ureters showed nothing remarkable; the bladder was contracted. The genitals appeared normal.

ANATOMIC DIAGNOSIS

Trephined opening in the skull, diffuse meningo-encephalitis, bilateral bronchopneumonia and pulmonary edema, syphilitic aortitis, chronic appendicitis and fatty liver.

SUMMARY

A man, aged 40, married, who had one living child, a negative family history, but an alcoholic personal history, who had no knowledge of any venereal disease, began to show lapses of memory in December, 1915, which increased in severity so that he was obliged to discontinue his work as a carpenter in the middle of 1916; he then became irritable, showed speech defect and became ataxic; in March, 1917, he received one intraventricular injection of arsphenamin through a trephined opening in the skull. He was admitted to the Manhattan State Hos-

pital in May, 1917, when he showed disorientation, poor memory, expressed grandiose ideas; showed marked speech defect, pupils were unequal and reacted very sluggishly to light, and the spinal fluid showed positive globulin, 54 cells, and a positive Wassermann reaction. He soon began to soil himself, became very euphoric and died following a convulsion. The postmortem examination showed the characteristic lesions of general paralysis in the brain; namely, a thickened pia showing a characteristic milky exudate in the anterior two-thirds, atrophy of the anterior poles of the cortex, lymphoid and plasma cells infiltration into the pia, neuroglia increases, cortical disorganization and perivascular exudation of lymphoid and plasma cells, many mast cells and a few rod cells, granulations on the floor of the ventricles, syphilitic aortitis and bilateral bronchopneumonia and pulmonary edema; the lesions in the left side of the brain which received the arsphenamin were more intense than those in the right side.

312 Hopkinson Avenue.

I am indebted to Dr. M. B. Heyman for allowing me to present and publish this case, and to Dr. F. C. Wood for the photomicrographs.

CONGENITAL TUMOR OF THE BRAIN (TELANGIECTASIS) AND ASSOCIATED CEREBRAL MOVEMENTS *

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PHILADELPHIA

The occurrence of congenital telangiectasis of the brain, diagnosed clinically and treated by operation is infrequent, and for this reason I have made a study of the case here recorded. It affords the opportunity to discuss associated movements of the limbs resulting from cortical defect.

REPORT OF CASE

History.—J. C., aged 12, was admitted to the University Hospital, June 17, 1918. The mother of the boy was exposed to roentgen rays when three and one-half months pregnant with this boy. Another child was held on the lap of the mother while it was being roentgen rayed. The birth of the patient was normal. When he was 2 or 3 months old his right upper limb was observed to be paralyzed, but it probably had been so from birth. The mother noticed when the child was about 1 year old that the right lower limb was paralyzed, because the child made no effort to crawl or stand. Since his birth he has had a telangiectasis of his forehead over the left eye, one in the left side of the scalp near the front hairline, a similar one in the left eyeball, and a small one on his back.

The first convulsion occurred May 1, 1918. This implicated the whole body and was with unconsciousness. The second attack occurred four weeks after this one and was general, and similar convulsions occurred later. He learned slowly at school and was backward in his classes.

Examination.—He wrinkles his forehead slightly. He closes both eyes well together, but cannot close either separately. In showing his teeth some weakness of the right side of the face is detected. The tongue is protruded awkwardly. He cannot close the right hand alone at all, but when he closes the left hand there is associated movement of the same kind with the right hand which the boy cannot prevent. Flexion at the left wrist and often even at the elbow produces a similar movement of the corresponding part of the right upper limb. The voluntary movement of the right upper limb at the elbow and shoulder is impaired. The movement at the right wrist is lost except in association with movement at the left wrist. The right hand is flaccid. The dynamometer registers 2 degrees in the right hand, 10 degrees in the left hand. The right upper limb is poorly developed and the right hand is much smaller than the left. Diadokokinesis is normal in the left hand and the test does not produce associated movements in the right hand. Stereognostic perception is lost in the right hand and the boy can tell only whether the object is cold or warm with this hand. It is normal in the left hand.

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* Read before the Section on Nervous and Mental Diseases at the Seventieth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1919.

He has imperfect movement in extension of the right lower limb and the power is not great. He cannot dorsally flex the right foot. Associated movements are present in the right toes. He cannot move the right toes alone, but when he moves the left toes the right toes move similarly, but associated movements are more pronounced in the right hand than in the right foot. He walks without difficulty.

Achilles and patellar tendon reflexes are exaggerated on the right side, normal on the left side. The Babinski reflex is doubtfully present on the right side, absent on the left. Temperature, touch and pain sensations are normal.

Operation.—Dr. Frazier operated on the patient June 26, 1918. A flap was made over the Rolandic fissure. On reflecting this, a dark-bluish discoloration with bulging of the brain appeared in the anterior and superior third of the opening, as though cavernous spaces of blood were beneath the dura at these places. The branches of the meningeal vessels were three or four times as large as they usually are and bled freely from the time the osteoplastic flap was reflected, and closure was attended with much difficulty. On incising the dura along the superior margin of the opening a tremendous venous channel was penetrated in which the blood welled until hemostatic clamps were applied. So much blood had been lost from various causes that no attempt was made to explore further.

Results.—July 24, 1918: The father reported that no convulsion had occurred since the operation. The boy has no increase of the right-sided weakness. He had a number of convulsions on July 29, but only one attack from this date to September 9.

April 11, 1919: His mother stated that his last convulsion had occurred in October, 1918, and was very slight. He had had no attack of any kind since and had been perfectly well, and had done well in school. Whereas formerly he had obtained very poor marks and had been observed to be deteriorating mentally, now he was bright and had recently obtained an almost perfect grade.

CASES MENTIONED IN THE LITERATURE

Angiomas have been classed by some as congenital tumors. The first case reported by Oppenheim in his paper on congenital brain tumor is the most interesting of his series. The patient had left hemianopsia since birth or early childhood. Sight had been absent in the left fields as long as he and his mother could remember; as a child he had not seen food or toys placed on his left side, and yet he seems to have had no other signs of cerebral disease until he was 18 years old. At that age he had severe headache, paresthesia, paralysis of the entire left side, etc. These symptoms disappeared leaving some weakness of the left side. When 25 years old he had a second attack consisting of severe headache and vomiting and lasting about 14 days. At 26 years he had a third attack similar to the first and became paralyzed on the left side. The diagnosis of a lesion of the right optic thalamus and the adjoining region was made. It was supposed to be a congenital tumor which caused focal symptoms at different periods because of transitory swelling or hemorrhage, probably an angioma cavernosum.

In three out of Oppenheim's four cases the symptoms began in adult life, in one at 18 years, in another at about 23 or 24 years, and in the third at about 33 years. The relative late onset of symptoms in angioma is striking, also the possibility of repeated hemorrhage in such a tumor, but all of his cases seem to have been without either operation or necropsy. An angioma of the face was found in two of the four cases, and Oppenheim mentions that experience has shown such a lesion is frequently associated with angioma of the cerebral meninges, and he refers to Kalischer, Emanuel, Bruns and himself in this connection.

He mentions as congenital tumors of the brain dermoid cysts, teratoma of the hypophysis, angioma, possibly cholesteatoma and neuroma of the brain nerves.

Fig. 1.—Porencephaly of the left cerebral hemisphere.

These congenital tumors may cause symptoms in early childhood, and then be latent many years, or produce symptoms with long intermissions, or the symptoms may first appear in later life.

Oppenheim had only twice been able by biopsy to confirm the clinical diagnosis of angioma of the brain, although he had observed angioma a few times at operation in cases in which he had made the general diagnosis of brain tumor. He does not distinguish sharply between angioma and telangiectasis.

In the first of the two cases reported by Ernest Sachs there were fever and convulsions confined to the left side of the body beginning three months after a fall. The possibility of hemorrhage from the

telangiectasis is suggested by this, although Sachs does not accept this as a factor. A left-sided paralysis developed also and disappeared in a month. Then the patient was well about one year and because of the reappearance of jacksonian convulsions an operation on the brain was performed. A huge bluish mass of vessels protruded when the dura was opened, and was so dense in places that the underlying cortex could not be seen. An attempt to remove this mass at a second operation resulted fatally.

The second case was that of a patient with a pale telangiectasis over the forehead. An angiomatous process was found in the dura, which on reflecting the dura was found to have numerous connections with the pial vessels. All the vessels connecting with the pial vessels were ligated and the dural mass was ligated above and below. Two days after the operation the patient had a violent convulsion, but since then had been well. It would seem as though this extensive ligation of the vessels had not had any permanent serious result.

Sachs found very few cases in the literature like his second case. He mentions that the process in all three of Cushing's cases was in the dura, and that Cushing does not mention the possibility that an identical process might occur on the cortex.

Sachs disputes the propriety of calling these tumors angiomas and quotes Virchow and Adami in support of this opinion. He emphasizes that a telangiectasis is a congenital dilatation of capillaries without any new-formed blood vessels, while an angioma is a new growth and only properly so-called when new blood vessels are formed. These distinctions are lost sight of in the literature. He also refers to the existence of telangiectasis elsewhere on the body, especially the face, and mentions that this was true of Pean's case and of Cushing's.

In the case reported by Castex and Bolo the lesion was designated by them as angioma venosum racemosum and extensive ligation of the vessels was followed by recovery. No writer so far as I know has spoken of the danger of extensive ligation, and yet I have seen serious symptoms result in two cases from this procedure. In one case a hemorrhage occurred into the brain, and in the other hemiplegia resulted. I would therefore suggest caution in tying many vessels at one time, in cortical telangiectasis.

In my patient the numerous angiomas of the surface in connection with symptoms of cortical lesion indicated that the latter probably also was of the same vascular character, and I advised operation with this probability in mind. The operation revealed extensive telangiectasis of the motor cortex. Caution was exercised by Dr. Frazier to avoid ligating too many vessels, and no complications occurred. I have observed two cases of teratoma of the region of the medulla oblongata both with successful operation — one by Frazier and one by Elsberg.

The associated movements of the right side, the paralyzed side, were very marked in the case I have described. Such movements are well known and are most pronounced when the paralysis has dated from birth. Very rarely associated movements occur in people otherwise normal, who are unable to use either hand without a corresponding movement of the other hand, and cases of this character are attributed to Damsch, Fragstein, and Brissaud and Sicard by Lewandowsky. I have seen two striking examples of this: one case was presented by Drs. C. W. Burr and C. B. Crow before the Philadelphia Neurological Society; the other was exhibited at the last International Medical Congress held in London, but I have never seen any report of this case published.

Fig. 2.—Another view of porencephaly of the left cerebral hemisphere.

The case presented by Burr and Crow was as follows: The patient, a man, had had the condition since infancy. Whenever he made any complicated voluntary movements with the fingers or wrist of either

hand the other hand involuntarily made the same movements. Very simple motions such as flexing or extending one finger could be made independently, but even then, as a rule, there was a similar simultaneous movement of the corresponding finger of the other hand. The condition was confined to the hand muscles and did not appear when the upper arm alone was used. The feet and toes were not affected. By strict attention he could prevent the unused hand from moving, but he could not, for any length of time, keep his attention fixed on what he was doing and on inhibiting the hand. He did his work as a seaman well until he was ordered to climb a rope. He demurred, and it was found that on letting go with the lower hand to reach for a higher grip on the rope he let go with the upper hand and fell.

In discussing this case, I suggested that each hand of this man was innervated from both sides of the brain equally or both were innervated from one side of the brain alone.

AUTHOR'S OBSERVATIONS

The central nervous systems from two cases in my possession throw light on the mechanism of these movements. Unfortunately, the clinical history is very deficient in each case, and I do not know whether associated movements were present or not. Both established the fact that the anterior pyramid on the side opposite to the lesion may be unusually large when the other anterior pyramid is absent from a congenital defect of the pyramidal tract of one side.

One was a case of *porencephaly*. The brain was from a low-grade boy, whose memory was fairly good, who sang, but never learned to read. He was partly paralyzed on the right side and never used his right hand. An opening extended into the left lateral ventricle, and the walls of this ventricle were continuous with the external surface of the brain (Fig. 1), and the base of the left frontal lobe presented a condition of agenesia. The anterior pyramid on the left side was absent (Fig. 3) so that no motor fibers could have passed into the cord from the left cerebral hemisphere through the anterior pyramid. The right anterior pyramid was unusually large. The fillet on the left side also was much smaller than that on the right side. Inasmuch as he was reported to have been only partially paralyzed on his right side, whatever limited voluntary power he had on this side must have come from the right cerebral hemisphere.

The second case was that of a man (G. S.) aged 66, who entered my service at the Philadelphia General Hospital, Jan. 24, 1916, a few days before I went off duty, and was never studied clinically by me.

He had left-sided palsy said to have dated from birth, but this had not prevented him from working. He was able to go about, but had very little use of the upper limb, and could not use the left hand.

Shortly before Christmas, 1915, he seems to have had a stroke, and he lost power in both lower limbs. His mentality was much impaired. The grip in the right hand was good.

A note was made Feb. 25, 1916, that he had partial paralysis of his upper limb and of both lower limbs, and was slowly regaining strength in the lower limbs. He died Aug. 2, 1916. A small area of softening was found in the upper part of the left lenticular nucleus and above it and was probably the cause of the attack in 1915. The lateral ventricles were dilated, but the right one was very much more so than the left. The right anterior pyramid was exceedingly small, while the left was abnormally large. The right lemniscus was also much smaller than the left.

Fig. 3.—The anterior part of the medulla oblongata from the case of porencephaly. The left anterior pyramid is wanting and the right anterior pyramid is unusually large. The left fillet is much smaller than the right.

The cervical region, on the whole, showed diminution in size of the left anterior horn and of the number of cells it contained. There were sections in which this distinction was not so evident. The left lateral column was considerably smaller than the right in the cervical region, but showed no signs of overgrowth of neuroglia. In the lumbar region it was impossible to make any such distinctions between the two sides of the cord. There was, therefore, a moderate hypoplasia of the left side of the cord in the cervical region.

In both these cases there was partial hemiplegia dating from birth, and in both the anterior pyramid on the side opposite to the lesion was

unusually large, while the other anterior pyramid was entirely absent in the case of porencephaly and exceedingly small in the case of hydrocephalus. It is reasonable to conclude that the intact pyramid contained homolateral motor fibers, and in this way some movement was still possible in the hemiplegic side. In 1895, while working in Dejerine's laboratory I made a study of the spinal cords in many cases of hemiplegia in which death followed the lesion in a comparatively short time—that is, in a period permitting the use of the Marchi method of staining—and was able to demonstrate degenerated fibers in both crossed pyramidal tracts, more in the side opposite to the lesion, in many of the cases, from an unilateral lesion of the cerebrum. This was evidence that the degenerated fibers came from the side of the brain in which was the lesion and indicated that each side of the brain supplied both crossed pyramidal tracts of the spinal cord, though in unequal degree.

COMMENT

It is interesting to note that the boy with telangiectasis of the cortex and pronounced associated movements developed convulsions which were not jacksonian but implicated both sides of the body. Probably these convulsions, like the voluntary and associated movements, originated in the right motor cortex. The loss of stereognostic perception of the right hand might be attributed to the lesion of the left parietal lobe, and it is interesting to recall that the lemniscus on the side of the cerebral lesion in the two cases with necropsy was very much smaller, as though the decrease in size might have been a form of retrograde degeneration or possibly a hypoplasia. I have seen a diminution in size of the lemniscus in several cases of lesion of the cerebrum.

The diminution of the whole right side of the body and limbs of this boy probably was in association with defect of the motor tract from the left cerebral hemisphere. The case of hydrocephalus showed some diminution in the size of the motor tract in the spinal cord from the right side of the brain. It is common to find arrest of muscular development in the paralyzed side in early acquired or congenital hemiplegia, and probably this is dependent on defect of the motor supply of the corresponding side. At birth the muscles may be developed independently of the motor nervous system, as von Leonowa first showed, but at a very early period of extra-uterine life—exactly at what period is not known—the motor nervous system takes control of the muscular system, and defect of the former leads to defect of the latter.

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DISCUSSION

Dr. H. H. Hoppe, Cincinnati: In a large experience I have seen but one case of telangiectasis of the cortex. This occurred in a boy previously well up to the age of 19, when he developed attacks of jacksonian epilepsy. The most careful examination carried on over a period of from three to four weeks failed to reveal any signs of disease of the brain as manifested through physical signs. There was no weakness of the right side of the body, and not even the slightest indication of the Babinski sign of the sole of the right foot. On account of the fact that the boy had jacksonian seizures, it was deemed advisable to lay open the cortex and this condition of telangiectasis was found. In the majority of cases that I have read of there is no evidence to show before operation what is going to be found in the cortex. In the second place, I wish to question seriously after you have found this condition of telangiectasis whether it is wise to do anything further or not. The danger of ligating the vessels which supply the cortex of the brain has to be considered. In the case I referred to, the boy was made distinctly worse by the operation. He developed a hemiplegia which prevented him from earning his living, which he had been able to do before, and the operation did not improve his epileptic seizures. In fact, six months afterward they returned, and were just as bad if not worse than they had been before. While we may be justified in laying open the cortex to establish the diagnosis under these conditions, I doubt whether it is wise to tie off the arteries.

Dr. William G. Spiller, Philadelphia: I think it is better to tie only a few vessels at the time of operation on telangiectasis of the brain, and, if necessary, to tie other vessels at a later operation. My patient was undoubtedly improved by operation, although recurrence of symptoms is possible. Often angioma of the brain cannot be diagnosed clinically, but angiomatous growths on the head or face should suggest that the lesion in the brain may also be angioma.

TREATMENT OF NEUROSYPHILIS BY ARSPHENAMIN INTRAVENOUSLY AND AUTO-ARSPHENAMINIZED SERUM INTRASPINALLY *

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For the past seven years cases of syphilis of the central nervous system admitted to Dr. S. W. Lambert's service at St. Luke's Hospital have been treated with arsphenamin intravenously and the intraspinal administration of auto-arsphenaminized serum. About fifty such cases have received this treatment during this period, the majority of which have been of the tabetic type. The twenty-one cases reported herein have been investigated and followed up to determine the efficacy of this type of treatment.

TECHNIC OF ADMINISTRATION

The technic employed is essentially that of Swift and Ellis as described in their original article on the subject. Neoarsphenamin has been the drug usually administered intravenously; the other products, such as neodiarsenol, arsenobenzol, and novarsenobenzol, have been used when the former drug became difficult to obtain. Nine decigrams of neoarsphenamin were administered intravenously. One hour later sufficient blood was withdrawn to obtain from 10 to 30 c.c. of serum. The serum thus obtained was centrifuged for one-half hour and inactivated at 56 C. for one hour and injected intraspinally the following day. In the early cases this serum was diluted with saline solution to 40 per cent., but since then the concentrated serum has been used.

REACTIONS OFTEN FOLLOW

Reaction to the intraspinal treatment has varied a great deal. The usual reaction has consisted of darting pains in the legs, beginning an hour or two after the introduction of the serum, and lasting from twelve to seventy-two hours. Associated with these pains there has sometimes been severe headache, girdle sensations, and disturbances of bladder control. The reaction in one patient (Case 3 in the table) was unusually severe. This patient, several hours after the intraspinal treatment, suffered from intense headache and severe lightning pains and loss of bladder control. His temperature rose to 101.2 F.,

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and he developed rigidity and retraction of the neck and a positive Kernig's sign. The following morning his white blood count rose to 31,000, with 95 per cent. of polymorphonuclear cells in the smear, and the cell count in the spinal fluid was 10,000, with 85 per cent. of polymorphonuclears. Cultures and smears of the spinal fluid were negative bacteriologically. Symptoms continued severe for five days and gradually abated. In a week the spinal fluid cell count fell to 75, and a month later it was 10, with 100 per cent. lymphocytes in the smear, and the patient was free from all pain or other after effects.

While in some instances very little discomfort is experienced, it is usual to have more or less discomfort for twelve or more hours following the intraspinal treatment. For this reason the following medication is ordered as a routine measure after such treatments:

		gm. or c.c.	
℞ Codeinae sulphatis.....		033	gr. ss
Acetanilidi		132	gr. ii
Acidi acetyl-salicylici sodii bicarbonatis.....	āā	66	gr. x

M. et fac pulveres v.
Sig.: A powder every three hours, for three doses, if needed.

We have been unable to demonstrate any relationship between the severity of the reactions and the dilution, or quantity of the serum injected, in amounts between 10 and 25 c.c. We are convinced, however, that cloudy serums due to the presence of an excess of fat or to hemoglobin are much more likely to give severe reactions than are clear serums. The presence of hemoglobin can be guarded against in part by the use of dry syringes, needles, and flasks, and care in seeing that the blood is not shaken up in transit to the laboratory. The presence of an excess of fat is more difficult to control, but the serums may be improved in this respect by having the patients fast for five or more hours before the blood is to be withdrawn.

SYMPTOMS IN THIS SERIES OF CASES

In the accompanying table the data concerning the symptoms presented in these cases have been recorded under three main heads: subjective and objective symptoms, and laboratory evidence. Subjectively, the most common symptom has been pain; after this, disturbances in gait; then disturbances in bladder control and vertigo. Objectively, 85 per cent. have shown pupillary disturbances, 76 per cent. a Romberg sign, and 52 per cent. an absence of knee jerks. Seventy-six per cent. have given positive blood Wassermann reactions, 76 per cent. positive spinal fluid Wassermann reactions, and 76 per cent. have shown an increase in globulin. Three cases gave positive spinal fluid Wassermann reactions and negative blood Wassermann reactions, and two cases showed the contrary condition.

RESULTS OF TREATMENT

It cannot be expected of any form of therapy that it will undo destructive changes which have already occurred. But this form of treatment may be expected to control associated meningeal inflammations. The control of an associated meningeal involvement is the best explanation we can give for the improvement which these cases have shown.

We have observed no instances among well defined tabetic cases where absent knee jerks have returned, or where sluggish pupils have regained their activity. We have been impressed by the frequent improvement in the ataxia of these cases as manifested by increased steadiness in gait and a decrease in the intensity of the Romberg sign. These cases almost uniformly show improvement in nutrition, several of them showing increases in weight varying from 16 to 31 pounds.

The most gratifying results from the treatment have been shown by its effect on the subjective symptoms. In spite of the fact that the intraspinal treatments often cause severe reactions we have found these patients more anxious to continue their treatments and to return to the hospital than any other class.

From this point of view, also, it is not usual to see a return to the condition of normality, but we have been struck in questioning these patients with the fact that in most of the cases there has been a very marked and sustained diminution in the amount of discomfort from which they were suffering before the institution of treatment. In almost every one of the cases here recorded there has been relief to a great extent from pain. Similarly there has been a frequent improvement in bladder function. Of six patients suffering from vertigo, in four the condition has disappeared under treatment, one has shown improvement, and in the sixth, the condition has become progressively worse in spite of vigorous treatment.

The influence of the treatment on the serology and cytology of the disease can best be seen by reference to the table. Here it will be seen that the blood Wassermann reaction has either been reduced in degree or changed to a negative reaction in all but two cases, in which it was uninfluenced. The spinal fluid Wassermann reaction has been reduced in degree or changed to a negative reaction in nine instances, has been uninfluenced in five cases, and in one case has become stronger during treatment. The globulin reaction has been reduced in thirteen cases, and has become stronger in five. Since the introduction of the colloidal gold reaction as a routine test in cases of nervous disease eight of the cases of this series have been tested by this means on each of their admissions. Two cases have shown positive gold curves in the absence of either a positive blood or spinal fluid Wassermann

reaction. One case has shown a positive curve with a negative spinal fluid Wassermann reaction, but a positive blood Wassermann reaction. All of the cases with positive curves have shown increases in the spinal fluid cell count and globulin content. Seven of the cases have shown a decrease in the intensity of the reaction after treatment. In the eighth case the curve assumed the paretic type during treatment and the patient developed general paresis clinically (Case 20).

As we have noted above, the majority of the cases were of the tabetic type. Two of the cases were spastic in type. One of these showed marked improvement after fifteen treatments with the disappearance of spasticity on the affected side, and a return of the reflexes to normal (Case 15). In another similar case of longer duration the patient has shown moderate improvement after fourteen treaments, and can walk with the use of a cane (Case 17). We have not undertaken the treatment of any paretic cases, but have had two cases develop paresis during or after treatment. One of these patients had received six treatments over a period of four months, the other had been under treatment for tabes for twenty-four months and had received seventeen treatments (Cases 20 and 21).

We have endeavored in the accompanying table to state graphically the essential data concerning the cases, using the plus sign to indicate the presence of a condition, and the zero sign to denote its absence, and using one, two, three, or four plus signs according to the relative intensity of the symptom.

We have selected the following group of cases to discuss in greater detail:

ILLUSTRATIVE CASES

CASE 3.—*History.*—F. S., a man, aged 48, had symptoms during a period of three years. He has had attacks of severe shooting pains in legs at irregular intervals, with difficulty in walking in the dark.

Physical Examination.—This revealed unimpaired sensations, equal but sluggish pupils, absent knee jerks, slight ataxia of legs, and positive Romberg sign.

Laboratory Findings.—The blood Wassermann reaction was positive; spinal fluid Wassermann reaction, positive; cell count, 4.

Treatment.—This patient had received one or two intravenous injections of arsphenamin before admission to the hospital. After admission he received two injections intravenously of 0.9 gm. of neoarsphenamin and two intraspinal injections of 40 per cent. serum. After the second injection he developed the severe reaction described in the beginning of this article. He was discharged from the hospital in March, 1913, and went to Alabama to live.

Results.—Three years later in reply to our inquiry his physician, Dr. F. G. DuBose of Selma, Ala., writes: "The patient has had six intravenous injections of arsphenamin since his discharge and injections of bichlorid of mercury in the intervals. These were given in the first year after leaving the hospital. Four blood Wassermann reactions in the past year have been negative. For nine months after leaving the hospital he suffered at intervals with pains in the calves of the legs. At the present time he is free from pain or other tabetic symptoms. No Romberg's sign; knee jerks are slightly exaggerated."

GENERAL CLINICAL SURVEY OF A SERIES OF CASES OF NEUROSYPHILIS TREATED BY ARSPHENAMIN INTRAVENOUSLY AND AUTO-ARSPHENAMINIZED SERUM INTRASPINALLY

Case No.	Duration of Symptoms in Years	No. of Treatments	No. of Months Treated	Subjective Symptoms				Objective Symptoms										Laboratory Evidence							
				Pain		Disturbance of Bladder Function		Gait		Pupils		Knee Jerks		Romberg				Blood Wassermann Reaction		Spinal Fluid Wassermann Reaction		Cells		Butyric	
				On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment	Weight: Lbs. Gain under Treatment		On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment	On Admission	After Treatment
1	8	10	39	+++	Much imp.	++	Improved	Ataxic	Much improved	A R	A R	0	0	+	+	16		±	±	±	0	10	—	+	0
2	4	5	5	+++	Improved	++	Improved	Ataxic	Improved	A R	A R	0	0	+	+	17		++++	0	+	0	22	10	0	±
3	9	2	1	+++	None	0	0	Slightly ataxic	Normal	Sluggish	Sluggish	0	+	+	0	..		+	0	+	0	4	10	+	0
4	12	4	2	+++	Improved	+++	Improved	Ataxic	Improved	A R	A R	0	0	+	+	Gained		0	0	++	0	9	3	+	0
5	6	18	15	++++	Improved	++++	Not improved	Ataxic	Slightly improved	A R	A R	0	0	++	++	..		++++	+	++++	++++	14	135	+	++
6	Several	4	3	++	Not improved	+	Not improved	Ataxic	Not improved	A R	A R	+	+	+	+	..		++++	++	++	+++	18	15	+	++
7	6	4	9	++	Improved	++	Improved	Ataxic	Improved	A R	A R	0	0	+	+	30		0	0	++++	+	13	40		
8	Several	6	10	++	None	0	0	Slightly ataxic	Improved	A R	A R	0	0	+	+	..		++++	..	+	+	25	5	+	0
9	1/12	5	3	++	None	0	0	Normal	Normal	A R	A R	++	++	0	0	..		+	+	+	+	12	35	0	
10	16	3	3	+++	Improved	+	Not improved	Ataxic	Improved	A R	A R	0	0	++	++	..		+	..	.	..	90	160	+	0
11	3	4	10	+++	Improved	0	0	Ataxic	Improved	A R	A R	0	0	+	+	..		+	0	+	0	5	3	..	0
12	10	9	9	+++	Improved	+	Not improved	Normal	Normal	A R	A R	+	+	0	0	..		+	0	±	±	76	5	+	0
13*	7	29	38	++	Improved	+++	Improved	Ataxic	Improved	A R	A R	0	0	++	++	31		0	0	0	0	59	4	+	0
14†	3	25	32	++	Improved	++	Worse	Ataxic	Improved	A R	A R	++	++	+	+	..		+	+	0	0	18	2	+	0
15‡	1/12	15	16	0	0	0	0	Spastic	Normal	Normal	Normal	R + + L +	R + L +	+	0	Gained		+++	0	+++	0	119	4	++	0
16	1/3	15	15	++	Improved	0	0	Normal	Normal	Normal	Normal	+	+	0	0	25		0	0	++++	0	40	0	+	0
17§	2	14	21	++	Improved	+	Improved	Spastic	Not improved	Normal	Normal	R 0 L ++	R 0 L ++	+	+	Lost 10		0	0	0	0	24	1	+	0
18¶	1/4	6	19	0	0	0	0	Normal	Normal	Sluggish	Sluggish	++	++	0	0	..		++++	0	++++	0	25	4	++	0
19#	1/4	6	6	0	0	0	0	Normal	Normal	A R	A R	+	+	+	0	22		++++	+	++++	++++	12	15	+	0
20‖	10	17	24	++	Improved	0	0	Ataxic	Improved	A R	A R	0	0	+	+	..		±	+	0	±	30	175	+	+
21‖	3/4	6	3	++	Not improved	0	0	Normal	Normal	A R	A R	+	+	0	0	..		+++	±	++++	++++	3	9	0	0

A R = Argyll Robertson.
* Vertigo cleared up under treatment; regained sexual power; paresthesias cleared up.
† Headache improved under treatment.
‡ Transitory attacks of blindness cured; headache cured; vertigo cleared up.
§ Vertigo and diplopia cured.
¶ Headache and diplopia cured.
# Vertigo and headache improved.
‖ Became paretic.

Case No.	Colloidal Gold																			
	On Admission										After Treatment									
13	2	2	3	3	3	1	1	0	0	0	1	1	1	1.5	1	1.5	0	0	0	0
14	1	1	2	2	2	0.5	0	0	0	0	1	1.5	1.5	1.5	1.5	0	0	0	0	0
15	0.5	1	1.5	3	3	1.5	1.5	0	0	0	1.5	1.5	1.5	1.5	1.5	0	0	0	0	0
16	2	2	2	2	1.5	1	0	0	0	0	1.5	1.5	2	2.5	1.5	1.5	0.5	0	0	0
17	1	2	3	2	2	0	0	0	0	0	1.5	1.5	2	1.5	0	0	0	0	0	0
18	1	5	5	4	3	2	1	1	0	0	1.5	2	2	2	1.5	0	0	0	0	0
19	5	5	5	5	5	2	2	0	0	0	5	5	4	3	3	2	1	0.5	0.5	0
20	1	1	3	3	3	2	1	0	0	0	5	4	4	3	2	1	0	0	0	0

The foregoing case is interesting because of the extremely severe reaction to one of the treatments and the improvement which occurred later, notwithstanding this reaction.

CASE 4.—*History.*—M. S., a woman, aged 40. Duration of symptoms twelve years. She has had attacks about twice a month of sharp shooting pains in lower part of back, radiating down sides of abdomen and into legs. Pains associated with nausea and vomiting. Recently gait has been so unsteady that she has been confined to her bed. She has frequent incontinence.

Physical Examination.—This showed a thin, pale, emaciated woman, legs wasted and thin, muscles relaxed. The right pupil was smaller than the left, neither pupil reacted. Knee jerks absent; area of diminished sensation in patch on anterior surface of right thigh, on lower anterior surface of left thigh, and on anterior surface of left leg.

Laboratory Findings on Admission.—Blood Wassermann reaction, negative; spinal fluid Wassermann, ++; cell count, 9; globulin test, positive.

Treatment.—She received four combined treatments in six weeks. At the end of this time her blood Wassermann reaction remained negative; the spinal fluid showed a negative Wassermann reaction, negative globulin test, and a cell count of 3.

Results.—This patient improved steadily after the institution of treatment. Interviewed in May, 1916, eleven months after her discharge from the hospital, she had gained much weight, and had partially resumed her housework. Pains still occurred but at much longer intervals, were of less severity, and unassociated with nausea or vomiting. Her bladder control was normal, and her gait, while still ataxic, was much improved, as evidenced by the resumption of her household duties. In reply to a letter of recent date, three years after the last interview, she stated that the improvement noted then had been sustained.

CASE 13.—*History.*—J. G., a man, aged 45, had symptoms that dated back three years. He complained of severe shooting pains in back and legs, unsteady gait, poor bladder control, and loss of sexual power.

Physical Examination.—Pupils equal, but react sluggishly; gait ataxic; marked Romberg sign; has to walk with two canes.

Laboratory Findings.—The blood and spinal fluid Wassermann reactions were negative; globulin test in spinal fluid, negative; cell count, 7.

Treatment.—This patient has been under treatment for thirty-eight months, and has received twenty-nine combined intravenous and intraspinal treatments. On his last admission in March of this year, the patient reported that he had had very little pain in the last three years; his sexual power had been normal for the past nine months; his bladder gave him very little trouble, and he had gained 31 pounds since beginning treatment. On admission his gait had been so ataxic that he had difficulty in walking with two canes without assistance. At present he uses only one cane, and can walk for a short distance without it.

The foregoing case has shown negative serologic tests throughout. Some observers are of the opinion that intraspinal therapy should be resorted to only in the presence of positive findings in the spinal fluid. We doubt very much if the same results could have been accomplished in this case by intravenous therapy alone.

CASE 15.—*History.*—W. B., a man, aged 29, complained of attack of unconsciousness one month before admission with subsequent transitory attacks of blindness; frequent attacks of vertigo and almost constant headache; weakness of the right leg. He had had a chancre and rash five years previously.

Physical Examination.—This revealed normal pupils with a right lateral nystagmus; convergence normal. All deep reflexes exaggerated on the right; ankle clonus and positive Babinski obtained on the right; Romberg positive; spastic gait with dragging of right leg.

Laboratory Findings.—The blood Wassermann reaction was +++; spinal fluid Wassermann, +++; cells, 119; globulin test, ++; colloidal gold curve, 05 1 15 2 3 15 15 0 0 0.

Treatment.—This case received twelve injections of mercury at the time of the secondary eruption. On admission the patient was put on mixed treatment and was given two intravenous injections of arsphenamin, 0.6 gm. each, and two intraspinal injections of concentrated arsphenaminized serum at intervals of two weeks. He was then treated as an outpatient, being admitted to the hospital once a month for intraspinal injections—fifteen in all. During the intervals he was given mixed treatment.

Results.—At the end of fifteen months this patient is now pursuing his trade as an electrician. The subjective symptoms have entirely disappeared; gait and reflexes are normal, and the serologic findings are negative. Monthly blood and spinal fluid Wassermann tests have been negative for the last five months. He has gained weight under treatment.

CASE 17.—*History.*—E. S., a woman, aged 39, complained of gradually increasing weakness of the right arm and leg, diplopia, generalized muscular pains and vertigo; difficulty in starting micturition. Duration two years. Has been married twice; no definite history of infection, although the patient believes her first husband had syphilis. One child living and well—later, one miscarriage.

Physical Examination.—This revealed normal pupils, right external strabismus; right knee jerk absent, left exaggerated; Romberg sign positive; gait spastic, bilateral Babinski reflex; no disturbance of sensations.

Laboratory Findings.—The blood and spinal fluid Wassermann reactions were negative; cell count, 24; globulin test, positive; colloidal gold curve, 1 2 3 2 2 0 0 0 0 0.

Treatment.—The patient remained in the hospital two months. During that time she received mixed treatment and two combined intravenous and intraspinal injections. She is now being treated as an outpatient, having received a total of fourteen treatments in twenty-one months.

Results.—At the latest visit she reported marked improvement with a returning use of right arm and leg. She does light housework. Gait still spastic; there is marked improvement in pain, vertigo, and bladder control. Has lost 10 pounds in weight. No strabismus; knee jerks and Romberg sign unchanged. Spinal fluid cells and globulin reaction are now normal, and colloidal gold curve is improved.

CASE 20.—*History.*—C. V., a man, aged 37, had symptoms during a period of ten years. He has had frequent attacks of pains in legs, and severe attacks of vomiting, unassociated with pain. Legs weak and gait unsteady. Vision in the left eye was poor.

Physical Examination.—This revealed Argyll Robertson pupils, absence of knee jerks, a moderate Romberg sign, well marked ataxia of lower extremities, and slight ataxia of hands.

Laboratory Findings on Admission.—The blood Wassermann reaction was doubtful, probably positive; spinal fluid Wassermann, negative; cell count, 30; globulin reaction, positive.

Treatment.—This patient received seventeen combined treatments in two years. Under the treatment his pains became less frequent and less severe in character and there was apparent improvement in his gait. A month before his last admission he began to develop delusions of grandeur, and on admission he was unmistakably paretic and had to be transferred to another institution.

The foregoing case is interesting in that treatment was begun at least a year and a half before the patient became of paretic type and that paresis developed in spite of the treatment.

CONCLUSIONS

In this series of cases 214 intraspinal treatments have been given. Severe reactions have occurred, particularly in Case 3, but we have seen no permanent injury or ill effects result from the intraspinal use of auto-arsphenaminized serum.

The treatment has uniformly been of benefit in its effect of increasing the patients' comfort by lessening the severity and frequence of their pains, in frequently improving bladder control, and in improving their nutrition. Improvement in station and in gait has frequently been observed in these cases, and in some, to a very marked extent.

PERNICIOUS ANEMIA WITH MENTAL SYMPTOMS

OBSERVATIONS ON THE VARYING EXTENT AND PROBABLE DURATION OF CENTRAL NERVOUS SYSTEM LESIONS IN FOUR NECROPSIED CASES *

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CINCINNATI

Our knowledge of pernicious anemia is being constantly enriched, especially our knowledge relating to the changes occurring in the nervous system. And justly so, because after all, next to the blood changes, the most characteristic and frequent clinical findings are on the part of the central nervous system. Minnich† (1893) demonstrated lesions in the spinal cord in approximately 70 per cent. of cases of pernicious anemia. Of forty-one cases treated by Billings (1900), forty showed neurological symptoms. In a very recent (1919) report of the 150 moderately advanced cases of pernicious anemia examined at the Mayo Clinic, Woltman found indisputable evidence of nervous tissue disintegration in over 80 per cent.

Formerly the neuropathology of this disease consisted chiefly in descriptions of the changes taking place in the spinal cord. It has been but comparatively recently that investigation has shown that these changes are not limited to the cord, but involve other parts of the central nervous system as well. (Pfeiffer, Barrett, Woltman.)

ETIOLOGIC FACTORS

In discussing the etiologic relationship between the brain and cord changes on the one hand and the blood changes on the other, one is confronted by various theories, each of which has its ardent supporters. The reason for this diversity of opinion is our ignorance of the fundamental cause or causes underlying this disease. Practically all are agreed that the clinical syndrome which we call pernicious anemia is produced by one toxin, the nature and origin of which, however, are still mooted points.

We feel safe in assuming that the disease is due to a toxin because of experimental work performed along similar lines in cases of anemia

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† Bibliography will be found at the end of the article.

due to the *Bothriocephalus latus*. It was long known that all individuals harboring these parasites did not develop pernicious anemia. Of those that did develop it nothing was disclosed either during life or at necropsy to show that they possessed any characteristics that might be regarded as predisposing them to this disease. The natural inference, then, was that the parasite was the variable factor. In other words, some change occurred which transformed the parasite from a harmless, though unwelcome, inhabitant of the intestinal tract into a deadly menace.

Elaborating on this idea, Shapiro advanced the theory that when the worm died or became diseased, noxious substances were produced which on being absorbed produced the anemia. The work of Wiltschur strongly supports this view. He examined twelve worms, the removal of which cured severe anemias and found that in "all cases the worms were either dead, decomposed, or sick."

Reasoning by analogy, we feel confident that the Addison-Biermer type of anemia is also due to a toxin. As to its origin, we as yet know nothing very definite. Much work has been done in this connection. The regularity with which changes occur in the gastro-intestinal tract, has led many to believe that this condition is essentially a disease of the gastro-intestinal tract (Grawitz-W. Hunter). Atrophy of the gastric mucosa, achylia gastrica, and intestinal stasis are frequently encountered. Berger and Tsuchiya found that extracts of the gastric and intestinal mucous membranes from patients dead of this anemia were more hemolytic than extracts of normal mucous membranes. This statement, however, is disputed by Ewald and Freidberger.

It is well known that certain chemical substances, such as oleic acid, saponin, phenylhydrazin, b-amino-azolyl-ethylbenzaldehyd and p-oxyphenylethylamin are capable of producing intense hemolysis. One of these substances, namely p-oxyphenylethylamin, has been isolated by Iwao from autolyzing pancreas, putrefying horse flesh and from Swiss cheese. Conceivably this compound may arise in the intestinal tract as the result of decomposition of food. Berthelot and Bertrand have shown that among the flora of the intestinal tract there is a bacillus, the *B. aminophilus*—which is capable of producing p-oxyphenylethylamin from tyrosin. Thus we can readily see how intestinal stasis could be a great factor in the production of pernicious anemia.

On the other hand, others have taken the stand that the increased production of hemolysins is due to a condition of hypersplenism. The toxin is carried by the blood to the spleen where certain changes occur. According to Moffit, "erythrolysis does not take place in the spleen but in some way the erythrocytes are sensitized and prepared for later destruction in the liver, marrow or lymph glands." From this view-

point it would be easy to account for the beneficial results that often follow splenectomy.

Granting that a toxin is responsible for this condition the lack of the fundamental knowledge as to its origin and modus operandi, makes it all the more difficult in trying to solve the causal relationship between the blood and the central nervous system changes. We have a mass of clinical and histopathologic data that has been accumulating ever since Addison first described pernicious anemia in 1855. Investigators have naturally tried to correlate these facts, and in correlating them, have advanced many theories. Most of these theories have long since fallen by the wayside; others, however, have remained and can be briefly summarized as follows:

1. A toxin produces the anemia which in turn produces another toxin that causes the changes in the brain and spinal cord.

2. The anemia itself acts as a toxin which through malnutrition causes the changes observed in the central nervous system.

3. The toxin acts independently on the blood and on the central nervous system.

Before discussing the relative merits of these theories it is essential to bear in mind certain well established facts. The absolute lack of correspondence between the brain and cord changes on the one hand and the anemia on the other hand both from anatomic and clinical standpoints has long been known.

Clinically there are many cases in which the neurological symptoms appear before the anemia. In other cases, both conditions arise simultaneously, and in still other cases, the anemia is present long before the appearance of any neurological disturbances.

Similarly, either condition may improve without a corresponding improvement in the other, or both may show a coordinate improvement.

Furthermore, it has been stated (Goebel) that cases that clinically show disturbances of the central nervous system may on section show no demonstrable organic changes.

From the above statements, it is obvious that the first two theories are untenable. So long as it is possible for the nervous symptoms to precede the appearance of the anemia, then it is impossible to maintain that the anemia either directly or indirectly, that is, through the production of another toxin, produces the cord and brain changes.

The third theory, however, overcomes this objection. If we assume that the toxin acts independently on the central nervous system and on the blood, then we can say that in one instance, the toxin acts first on the central nervous system and then on the blood, thus producing those cases in which the disease is ushered in by the nervous symptoms. In another instance, it acts on the blood first. These are the cases in

which the anemia precedes the development of neurological symptoms. In still another instance, the toxin acts simultaneously on the central nervous system and on the blood, thereby giving rise to a clinical picture showing both brain and blood changes at once. (Nonne-Billings.)

So far so good. But, on the basis of this theory, how can we explain the fact that in cases where similar therapeutic measures, for example, splenectomy, have been instituted, some will show an improvement in the neurological symptoms without any improvement in the blood picture, while others, reversely, will show a betterment in the anemia without a corresponding betterment in the cord and brain changes.

Decastello * performed a splenectomy on a patient who had suffered from the disease for less than a year. The anemia was severe and the spleen but slightly enlarged. Since the operation, the patient has shown marked improvement clinically but with no alteration in the blood picture.

Harpole,* on the other hand, performed a splenectomy on a patient who had been known to have had the disease for at least two years. The anemia was moderately severe. Following the operation there was an immediate improvement. The patient has continued in fair health with only a slight anemia but with *persistence of the spinal cord symptoms.*

Furthermore, how will this theory account for those cases which showed clinical evidence of involvement of the central nervous system, but in which the pathologist, on necropsy, is unable to discover any demonstrable lesion?

It seems to me that if we judiciously combine the second and third theories into some such theory as the following, we shall have one that will account for all of the various manifestations of pernicious anemia. Briefly stated it would read as follows:

1. One toxin produces pernicious anemia.

2. This toxin acts independently on the blood and on the central nervous system.

3. The anemia itself, after it has persisted for a considerable length of time, interferes with the metabolism of the nerve cells, thereby indirectly enhancing the poisonous action of the toxin so that instead of being merely an irritant to the nervous tissue, it becomes a highly destructive agent. In this way, the changes which at first were purely temporary and functional now become permanent and organic.

In other words, I think that we can with justice assume that the nervous structure is open to two lines of attack, namely, (1) a direct or frontal attack by the toxin, and (2) an indirect or flank attack by

* See Pearce, Krumbhaar and Frazier: The Spleen and Anemia.

the anemia. If the anemia is improved before the latter attack has materialized we get an improvement in the neurological symptoms and such a patient on necropsy will show no pathologic cord or brain lesions.

If, however, the anemia has persisted long enough for both frontal and flank attacks to materialize, then improvement in the blood picture will not be followed by a corresponding improvement on the part of the central nervous system. Such cases coming to necropsy will show the changes that are usually found in the cords and brains of pernicious anemia patients.

This theory is in line with the views of Bonhoeffer who thinks that the psychoses that some patients present are not due to the direct action of the toxin but to the interposition of some metabolic changes in the nerve cells.

Christian's recent work strengthens this view also. He tested the renal function in fourteen cases of pernicious anemia and found that the latter produced a chronic nephritis which could be improved by improvement of the anemia, provided the latter had not persisted for too great a length of time. His conclusions are:

> In patients with pernicious anemia the disease is accompanied by a disturbance of renal function, as measured by renal dietary tests, which is similar to that found in patients with advanced chronic nephritis. In these patients there is no other evidence of chronic nephritis and the disturbance appears to be due to the anemia, decreasing with the subsidence of the severity of the anemia *unless the anemia is maintained so long that a permanent disturbance of renal function ensues.* [Italics mine.]

This theory stated in its entirety would read as follows:

1. One toxin causes both the blood and the central nervous system changes.

2. This toxin acts independently on the blood and on the central nervous system. This would account for those cases in which (*a*) the neurological symptoms manifest themselves before the anemia, or (*b*) in which the anemia precedes the brain and cord changes, or (*c*) in which both conditions arise simultaneously.

3. As soon as the typical blood picture of pernicious anemia develops and persists for a considerable length of time, the metabolism of the nerve cells is so impaired that the changes which were purely functional at first and due to the irritating action of the toxin alone, now become organic and permanent. Hence, no matter how greatly the physical state is improved, be it through splenectomy, transfusions, or drugs, no improvement on the part of the nervous system follows. The damage is irreparable. If, however, the hemolysis has not lasted very long, then improvement in the neurological symptoms may be expected to follow the exhibition of proper therapeutic measures. We can thus

account for the apparent contradictory results in the cases reported by Decastello and Harpole. In the latter case, the anemia had lasted for at least two years. Removal of the spleen was followed by an improvement in the blood picture but with no improvement on the part of the central nervous system. Here we can rightly assume that the anemia had interfered to such an extent with the metabolism of the nervous elements that permanent lesions had been produced.

In the former case, the anemia had existed for a much shorter period and therefore splenectomy was followed by improvement in the neurological symptoms.

In line with this theory is the fact brought out by Pearce, Krumbhaar and Frazier and their co-workers, that if splenectomy is performed before the blood has reached an extreme degree of deterioration, not only is the operative risk lessened but the improvement is greater and more lasting.

Finally, on the basis of this theory it is easy to account for those cases which during life showed clinical evidence of involvement of the central nervous system but which on necropsy showed no lesion, either in the cord or brain. In these cases, the irritant action of the toxin had not been aided by the anemia.

MENTAL SYMPTOMS OF PERNICIOUS ANEMIA

Many observers have called attention to the mental symptoms that frequently occur in pernicious anemia patients. The early investigators simply noted the somnolence, apathy, and coma that usually preceded the fatal termination of the disease. Later, however, it was noted that the mental symptoms were not simply terminal but that in a great many cases they constituted a dominant part in the clinical picture. Marcus and Langdon have each reported cases in which the mental changes appeared before the anemia or, at least, before the blood picture was sufficiently developed to warrant the diagnosis of pernicious anemia. Langdon termed these cases "prepernicious anemia." The psychic disturbances may range from mild depression to violent maniacal outbursts. Some cases will show irritability, hyperkinesis, delusions and hallucinations. Other cases will show indifference, apathy, and severe melancholia. Whenever a distinct psychosis, such as manic-depressive insanity, is present, the majority of observers look on it as separate and distinct from the pernicious anemia. At most, in such cases the pernicious anemia may be regarded as a predisposing factor. At present it is generally accepted that the psychotic manifestations should be classified with the exhaustion and toxic-infectious psychoses. Barrett expressed it very clearly when he said:

As to the clinical position, it would seem that they must be placed among the paranoid conditions which are symptomatic of a toxic organic process affecting the central nervous system—analogous to the paranoid conditions which have been noted in tabes, alcoholism and from certain drugs.

It has been but comparatively recently, however, that efforts have been made to link up the mental disturbances with the cortical changes. Barrett found many pathologic changes in the cortex but as a whole, not of the specific type. They appeared to be rather similar to those changes which occur in conditions of chronic intoxication, due, for example, to chronic alcoholism. The blood vessels showed the most constant changes. These were in the nature of swelling of the intimal cells and in some active proliferative changes. The most important findings, however, are the focal lesions, which correspond very closely to the lesions so characteristically present in the cord.

Woltman made a very thorough and exhaustive study of seven cases. His findings led him to the conclusion that the brain and cord changes run fairly parallel and with about the same frequency; and, furthermore, that patients who show degenerative changes in the spinal cord at necropsy, usually show the same type of lesion in the brain also. In the medullary substance of sections of different levels of the brain, he also found areas of degeneration of the Lichtheim type that are identical with those that are usually found in the posterior and lateral columns of the spinal cord. In addition to these focal areas of degeneration he noticed diffuse areas of degeneration in the long association tracts and in the short commissural fibers that pass from one gyrus to another. He calls attention to the fact that the gray matter shows involvement of a focal nature also, the cells of the marginal gray layer being principally involved.

REPORT OF CASES

Technic.—The following report is based on the study of four cases. In each case the brain and spinal cord had been fixed in formaldehyd solution and cut in the frontal plane. Blocks of tissue about 5 mm. in thickness were taken from each of the following regions: (1) left motor area; (2) middle of pons; (3) middle of medulla; (4) cervical region of cord; (5) dorsal region of cord; (6) lumbar region of cord. In addition, sections were also taken in some cases from the right motor area, the left internal capsule, and the peduncles. These were selected because, macroscopically they seemed to offer promising material for study. These blocks were then mordanted, embedded in parlodion, cut, under alcohol, into sections 25 microns in thickness and stained by the Weigert method. Those stained with cresylecht-violet, had formalin fixation and paraffin embedding and were cut into sections 6 microns in thickness. Some of the sections were also stained with hematoxylin and eosin.

Case 1 (Necropsy 15-106).—*History.*—O. D., a white man, aged 75, was admitted to the psychopathic department, Boston State Hospital, Sept. 27, 1915. He was mentally confused and had hallucinations and delusions of various kinds.

Family History.—The family history is entirely negative. There is no history of nervous or mental diseases in any of the collaterals.

Personal History.—The patient was born in Germany and had the ordinary diseases of childhood. He had a severe attack of rheumatism sometime between the ages of 50 and 60 years. About four or five years ago he began to have bladder difficulties. He left school at the age of 15 and spent the next twenty-six years at sea. He then came to this country and worked steadily for a ship concern until the onset of the present illness, which prevented him from performing his duties properly. His daughter stated that he left his work because his mind gave out and because he had dizzy spells and would fall on the street. His condition gradually became worse and he had begun to dislike people, preferred to stay alone, was irritable and ugly. He was always complaining and found fault with everything. He had delusions of persecution. His daughter had become afraid of him because of his ugliness. For the past three years he had been very pale and complained of numbness of the feet. However, he did not drag his feet.

Fig. 1 (Case 1).—Section of left motor area, showing areas of degeneration in close proximity to the blood vessels. One, in the upper right hand corner, is at the point of bifurcation of a capillary. In the upper left hand corner a focus of degeneration is seen surrounding blood vessels. Weigert's myelin sheath stain. Magnified about 40 diameters.

Ten weeks before admission, the patient fainted and afterward had a chill, a period of vomiting and later, fever which reached 102 F., after which he had a peculiar cold period. It seems that the mental confusion, hallucinations, rambling and incoherent talk have chiefly developed since the onset of this attack of chill, vomiting and fever. Previously he had always been constipated but during this bed-ridden period there was diarrhea and he had no control of rectum or bladder.

His hallucinations varied. At one time he saw a man in the room with him, sitting with his hat on; at another time, he saw trucks and a steamer in his

room. At times he feared that he was going to be put down into the cellar, and at other times he thought he was being kept there. He also had periods of memory defect.

Examination.—On examination, the face was seen to be puffy and pasty and the skin unduly pale. There was a sytolic murmur at the apex which was feebly transmitted to the axilla. The aortic second sound equaled the pulmonic second sound. The pulse was regular and of good volume. The blood pressure was: systolic, 130; diastolic, 70. The breath sounds were faint and crepitant; râles were heard all over the back and front. The liver was enlarged but not tender. The spleen was not palpable.

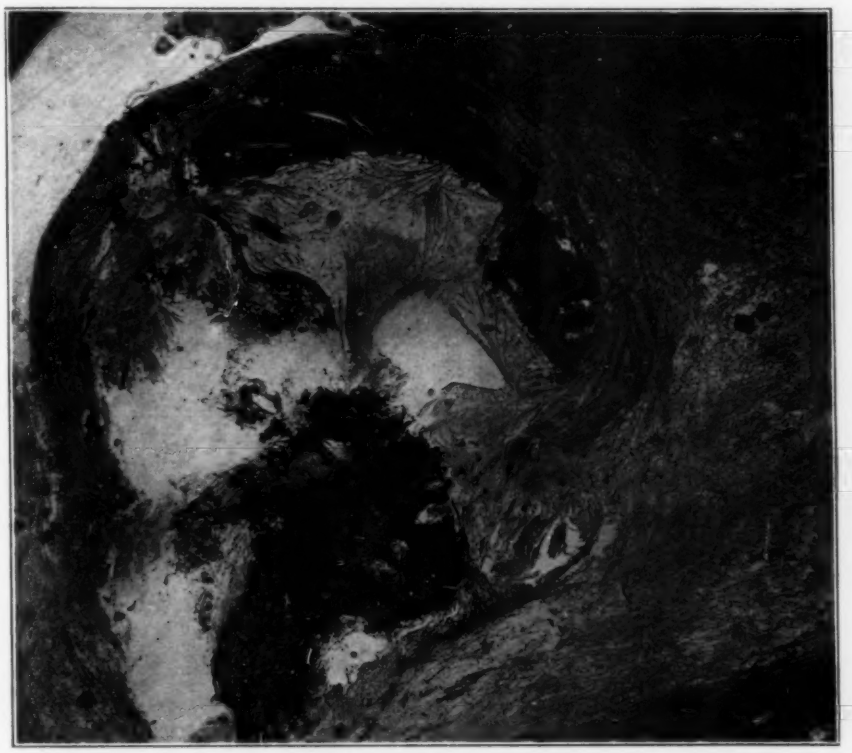

Fig. 2 (Case 1).—A large area of softening in the cortex produced by rupture of a large blood vessel. Weigert's myelin sheath stain.

Neurologic examination showed normal reacting pupils. The fundi could not be examined on account of the patient's restlessness. The triceps and biceps were present and equal on both sides. The abdominal reflexes were only obtained in the left inguinal region. Both knee jerks were absent. The same was true of the Achilles reflex. There were no Babinski, Gordon or Oppenheim reflexes. There was no ankle clonus. The deep sensibilities were not tested because the patient could not cooperate.

The urine showed a slight trace of albumin and an occasional red blood corpuscle, and a few granular casts and a rare hyaline cast. The blood Wassermann reaction was negative. Examination of the spinal fluid showed the

following: Fluid, clear; albumin, +++; globulin, ++; cells, 4; small lymphocytes, 100 per cent. Colloidal gold chlorid test, 0000000000. Blood Examination: This revealed the following: Hemoglobin, 30 per cent. (Sahli) with a color index of 1.66; red blood cells, 2,528,000; white blood cells, 4,600. A differential count (100 cells) gave polymorphonuclear leukocytes, 71 per cent.; small lymphocytes, 16 per cent.; large lymphocytes, 10 per cent.; eosinophils, 3 per cent.

There is a great variation in the size of the red blood cells with a large percentage of macrocytes. Poikilocytosis is marked. No achromia.

Course.—September 28: Patient has been lying quietly all day in a semicomatose condition. He does not comprehend questions, rarely speaks, and when he does, cannot answer questions relevantly. His mind wanders deliriously, calling for "Annie" and telling fabulous tales.

Fig. 3 (Case 1).—A so-called Lichtheim plaque in the left internal capsule. Weigert's myelin sheath stain.

September 30: Condition the same. The skin is very pale and has a slight lemon yellow tint. Both knee jerks and Achilles are absent. All the toes were drawn up on stroking the sole of the foot and in testing for Oppenheim's sign.

October 1. The patient has continued in the same low grade semiconscious semidelirious condition previously noted. He continues to call deliriously for "Annie," but otherwise makes practically no intelligent remarks, occasionally rambling about "the boat." The yellowish tint of the skin is more marked. Moist, bubbling râles could be heard all over the chest. Patient failed rapidly and died early in the afternoon.

Necropsy.—This was performed six hours after death. The body is that of a well built and nourished, white male, 176 cm. in length. The skin is waxy

gray with a slight yellowish cast. There is a faint edema of the lower legs and some atrophy of the left thigh. The pupils measure 5 mm. in diameter and are equal. There is a superficial decubitus over the sacrum. Rigor mortis is faintly present.

Fig. 4 (Case 1).—Here the miliary foci described by Preobrajensky are very conspicuous. The contrast between them and the larger so-called Lichtheim foci, three of which are also shown in this picture, is very striking. The foci of Preobrajensky are much smaller, more numerous and more sharply defined than the Lichtheim plaques. Although not shown in this photograph, in a good many cases an undamaged nerve fibril may be seen traversing a small focus. Weigert's myelin sheath stain of pons.

Ventral Section: The fat is lemon yellow in color and measures 2 cm. over abdomen and 1 cm. over thorax. The spleen is adherent to the external lateral surface. The appendix above the pelvic brim measures 7 cm. in length. The bladder is distended and the intestines somewhat injected. The diaphragm arches to the fourth rib on the right side and to the fifth interspace on the left side. The gallbladder is distended and contains many stones.

Thorax: The bone marrow is yellowish pink in the sternum. There is no free fluid in either pleural cavity, but there are adhesions at the apex of the right lung. The pericardium is heavily loaded with fat. The apex of the heart is in the fifth interspace.

Heart: Weight, 453 gm. The epicardial fat is fairly abundant. The descending branch of the left coronary shows sclerosis. The right coronary and circumflex arteries show constrictions with calcifications. Every valve is

Fig. 5 (Case 1).—Another view of a different section of the pons. The relationship of the large plaques of degeneration to the blood vessels is very clearly shown. Here we see again the formation of an area of degeneration at the bifurcation of a capillary. A large number of the smaller foci are also present. (Weigert method.)

thickened, particularly the aortic which shows distortion of the cusps. There are some vegetations which are calcified around the origin of the left coronary in the internal surface of the aorta. The myocardium is pinkish gray in color and contains multiple white streaks measuring from 0.5 to 0.6 cm. in extent.

Lungs: Weight—left lung, 385 gm.; right, 1,200 gm. The right lung pits on pressure, but is crepitant for the most part. There is a slight thickening

of the pleura at the apex. The bronchi are reddened and show frothy fluid adherent to mucus.

The left lung has a collapsed area in the lowest part of the upper lobe and in the posterior part of the lower lobe. Section of this shows it to be somewhat redder but not wetter than usual. The bronchi are reddened but the peribronchial lymph nodes are not enlarged.

Figs. 6, 7, 8 (Case 1).—Sections of the cervical, dorsal and lumbar regions of the spinal cord. The degeneration of the posterior columns is marked. This degeneration is only moderately severe in the lumbar region, but becomes progressively worse in the upper portions of the cord. It reaches its climax in the cervical region. Here, the destruction is seen to be very severe. Within the area of degeneration, large, jagged holes are present. This is in marked contrast to tabes dorsalis. In the latter condition, the degeneration of the posterior columns, as a rule, is greater in the lumbar region than in the cervical region. The degeneration in the lateral columns, which as a whole is much less than in the posterior columns, increases in intensity from above downward. The posterior roots in the lumbar section show evidences of degeneration. The hole seen in the lateral column of each section has been made to mark the right side of the cord. This applies to all the following photographs of the cord. Weigert's myelin sheath stain (× 10).

Spleen: Weight, 165 gm. There are two fetal lobulations on the lower border. The capsule is somewhat thickened and wrinkled. The pulp is red and watery, and retracts on section. The trabeculae are increased and the malpighian bodies are numerous.

Adrenals: They are embedded in fat and are large. On section they show marked mottling of cortex and medulla with yellow and red. The medulla is scarcely to be differentiated from the cortex.

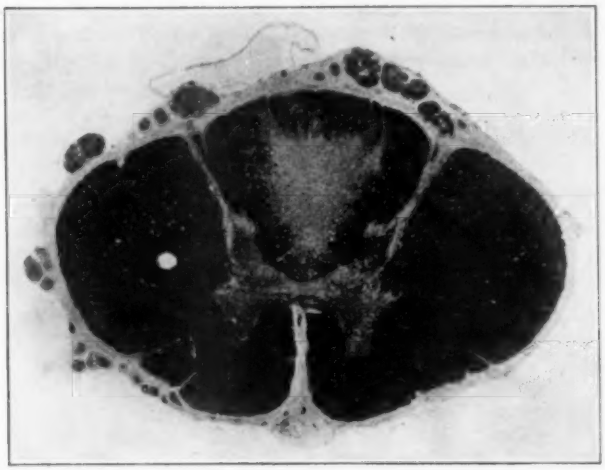

Figure 7

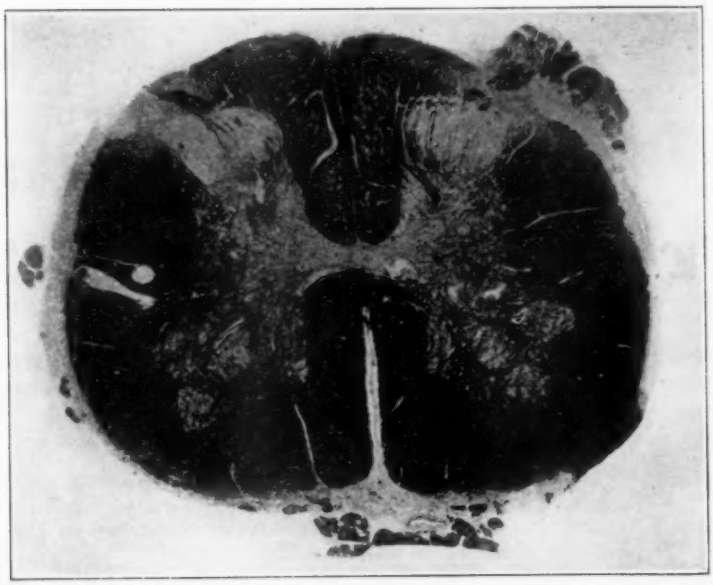

Figure 8

Kidneys: These are deeply embedded in fat. The capsule strips with difficulty.

Liver: Weight, 1,800 gm., and has a yellowish pink color. The capsule is slightly thickened and there is a focal area of adhesion to the diaphragm. Section shows a fairly pale homogeneous substance. The gallbladder contains forty-eight stones.

Pancreas: The splenic artery is tortuous, markedly sclerosed and calcified. Every level of the pancreas examined shows fat replacement in varying amounts.

Gastro-Intestinal Tract: Section of stomach shows the wall somewhat thickened and glossy. No rugae are present. Yellow mucus drips from the surface. There is nothing of note in the intestinal tract.

Special Examination: The bone marrow of the left femur was inspected, and found to be raspberry red in color.

Brain: The dura is very adherent, but not particularly thickened. The superior surface of the brain generally is firmer than normal. The convolutional pattern is rich. The pia mater is not thickened except slightly in the sulci over the vertex.

Base of brain shows a small aneurysm in the middle part of the left posterior communicating artery. The fourth ventricle shows clear granulations. The brain weight is 1,100 gm. which, according to Tigges' formula, shows a loss of 308 gm. The cord shows minute specks of translucency in the middle of the posterior columns.

COLLOIDAL GOLD CHLORID REACTION

	1	2	3	4	5	6	7	8	9	10	
Cortex	1	2	2	2	2	2	1	1	0	0	Bloody
Right base	1	2	1	1	1	1	0	0	0	0	Bloody
Left base	3	2	2	2	1	1	0	0	0	0	Bloody
Third ventricle *	0	0	0	0	0	0	0	0	0	0	
Spinal fluid	0	0	0	0	0	0	0	0	0	0	
Pericardial fluid	0	0	0	0	1	1	1	2	2	3	

Histologic Examination.—Weigert Sections—Left Motor Area: Macroscopically, one sees a cross-section of a very large blood vessel with thickened walls. Surrounding it, in the medullary substance, is a very large area of softening which shades off gradually into the surrounding normal tissue. On microscopic examination, this area of softening is seen to be composed of destroyed nerve fibers, with here and there, small patches of neuroglia and intact nerve fibers. The entire part appears cribriform owing to the presence of many large vacuoles some of which have apparently run together to form large cavity-like spaces. In the medullary portion, the blood vessels are thickened, the perivascular spaces are dilated and in a great many instances there is a thinning out of the myelin sheaths in their immediate neighborhood. In many cases, this destructive action has gone on to complete degeneration so that irregularly circumscribed areas which vary in size and structure have been formed. Some are filled with debris and crossed by a few undegenerated nerve fibers, while others are clear and hyaline-like in appearance. At the bifurcation of one of the capillaries there is a so-called Lichtheim focus. In the cortical area the blood vessels are numerous and have very thick walls. Some are seen to be ruptured. The perivascular spaces are greatly distended.

Internal Capsule: Here there are also vascular changes both in the gray and white matter. Many plaques of different sizes and shapes are seen sur-

rounding the blood vessels. The perivascular spaces are uniformly distended. In a small portion of the medullary substance one can see a few of the miliary foci described by Preobrajensky.

Pons: The most striking feature in this section are the miliary foci of Preobrajensky. They are very numerous and confined entirely to the medullary portions and are most numerous in the center. Practically all are of uniform shape but not of uniform size, some being three times as large as others. The smallest are about the size of small lymphocytes. They are fairly definitely circumscribed and have a punched out appearance. In many, an undamaged nerve fibril may be seen passing through the destroyed area. In addition to these miliary foci of Preobrajensky there are quite a number of well defined Lichtheim plaques. These bear a close relationship to the blood vessels.

Cord: With the unaided eye one can see a distinct circumscribed degeneration of the column of Goll. In the cervical region, this has proceeded to apparent cavity formation. The degeneration, although still sharply defined in the thoracic region, becomes less and less marked as we pass to the lumbar region. The reverse, however, is true of the lateral columns. Here the degeneration, which is much slighter than in the posterior columns, increases from above downward. On microscopic examination, we see that the column of Goll is practically entirely destroyed. Several large spaces with irregular jagged edges are conspicuous. Smaller vacuoles are numerous. Here and there are evidences of small hemorrhages. The blood vessels are intensely congested.

Cresylecht-Violet Sections—Left Motor Area: The pyramidal cells appear shrunken and granular. Many of the pericellular spaces are filled with a large number of satellite cells. The perivascular spaces, especially those of the cortical area, are distended.

Internal Capsule: Here and there are small islands of sclerotic tissue, apparently not related to the blood vessels. The pyramidal cells are uniformly shrunken, irregular in outline, and in a great many, the nucleus is displaced. Some satellitosis is present. From one pericellular space, the nerve cell had entirely disappeared and its place is occupied by five satellite cells.

Pons: Small, clear, oval areas corresponding in size and position to the miliary foci of Preobrajensky, seen in the Weigert section of the pons, are also present here. In the gray matter there are many small patchy areas of degeneration. The nerve cells are not as noticeably abnormal as those of the preceding sections.

Medulla: Pigmentation of the nerve cells is marked. The perivascular spaces are tremendously distended and filled with debris. Large areas of degeneration are present in the white matter. The pyramidal tracts are full of vacuoles. Two types of glia cells, differing principally in size, were observed. The larger ones, in all probability, simply represent more mature forms. They are profusely distributed over the entire section but more particularly in the region of the olivary nuclei.

Cord: The posterior columns contain numerous thin walled capillaries which are surrounded by large amounts of glia cells and fibers. The glia replacement cells are of comparatively large size and of the stellate type. An occasional undegenerated or only partially degenerated nerve fiber is seen. The increase in the number of blood vessels is most noticeable in the dorsal portion of the cord. The nerve cells show various changes. Some are very much shrunken and irregular in outline; others contain numerous variously-sized granules; still others are swollen and contain a large amount of yellow pigment. Pigmentation is present both in the anterior and posterior horn cells, but occurs

more frequently and uniformly in the former. This pigmentation differs from that normally found in the cells of persons of advanced years, in that it is diffuse, somewhat granular and not clumped at one pole of the cell body. In these cells, the pigment is centrally located and apparently has pushed the protoplasmic substance to the extreme periphery of the cell. In some of the cells, the nucleus is displaced to one side and stains poorly.

CASE 2 (Necropsy 16-59).—*History.*—C. C., a white woman, aged 54, was committed to the Boston State Hospital, April 25, 1916, with the diagnoses of pernicious anemia and symptomatic psychosis.

Family History.—Her mother died at the age of 50 of tuberculosis. Of six siblings, two have died of tuberculosis; one is now in a hospital suffering from tubercular trouble; one (a sister) is excessively alcoholic and has seizures with unconsciousness, and one died in infancy.

Personal History.—The patient was born at Salem, Mass., in 1862. Her education was limited but she was able to read and write. She drank a little beer and smoked cigarets for about a year. She formerly used snuff. Her sexual habits, as far as could be ascertained, were normal. She was never very cheerful, and many times greatly depressed. She was somewhat obstinate, but in many ways showed that she could be very sympathetic and kind. She was known to be hypochondriacal and apprehensive. She was a good housekeeper, was sociable and made friends. Her first marriage occurred when she was 18 years old. By that husband, she had one child, who died at the age of 3 of "water on the brain." At the age of 36, she was again married, but by this marriage she had no children and no miscarriages. Since the second marriage she has led a very lonesome life.

Medical History.—In childhood she was at the Salem Hospital because of anemia. According to the statements of her acquaintances, she has always been pale. She always claimed that she was a spiritualist and "could see dead people." Early in 1915, she went to the Eye and Ear Infirmary because she thought that she had cancer of the throat. In May of that year, she was for nearly three weeks a patient at the Massachusetts General Hospital with what was diagnosed as pernicious anemia. At that time she was irrational and had visual hallucinations. She saw animals and would point her fingers at imaginary objects. She walked unsteadily and fell frequently but never lost consciousness. Sometimes she had complete loss of vision for a few minutes. Until a year previous to this atttack, the patient was able to do her housework. Six weeks ago she became much worse; very excitable, swore and used obscene language. Recently she carried on an imaginary conversation with her deceased daughter. She has also turned against her niece and niece's little girl of whom she has been very fond. On occasions she would "jump out of bed at people." There were no homicidal or suicidal tendencies.

Physical Examination.—The patient was a well developed and well nourished woman of 54. Her face was of a striking pallor with a lemon yellow tinge. The mucosae were very pale. There was a harsh systolic murmur at the apex that was transmitted upward to the axilla. The liver was enlarged but not tender. The spleen was palpable in the left hypochondrium and the dulness extended to 3 cm. above the umbilical line. The blood pressure readings were: systolic, 105; diastolic, 45.

Neurologic Examination.—The pupils were equal and regular. They reacted well to accommodation but very sluggishly to light. There was no nystagmus or strabismus. The tongue protruded in the midline and appeared very anemic. The arm reflexes were all hyperactive. There was hyperesthesia of the lower

extremities. The knee jerks were equal but sluggish; the Achilles active and equal, and the plantars hyperactive. No Babinski, Gordon or Oppenheim reflexes were obtained. There was no ankle clonus.

A formal mental examination could not be made on account of her mental state. The patient appeared to be in a dazed, half asleep state. It was difficult to get her to comprehend questions but when her attention was gained, she usually answered the questions fairly well. When asked where she was born, she delayed before answering, then asked what the question was. She finally said that she was born in Salem. She did not know how long she had lived there. She answered questions as if very weary and gave the impression that the incorrect answers were due, in part, to lack of effort. She persisted in the feeling that her niece had intended to injure her and refused to see her.

Fig. 9 (Case 2).—Weigert's myelin sheath stain of left motor area showing small foci of degeneration and one larger area in intimate relationship with the neighboring blood vessels.

Her condition gradually grew worse and she was less and less easily aroused. Twelve days after her admission, she died.

Wassermann Reaction: Serum, negative.

Blood Examination: Hemoglobin less than 10 per cent. (Sahli); color index, 1.6; red blood cells, 780,000; white blood cells, 4,700; polymorphonuclear leukocytes, 60 per cent.; small lymphocytes, 32 per cent.; large lymphocytes, 8 per cent. The red blood cells showed marked anisocytosis and poikylocytosis, and some achromia. There was a large number of microcytes and macrocytes. No stipling or nucleated reds were seen.

A later blood examination showed hemoglobin less than 10 per cent. (Sahli); red blood cells, 550,000; white blood cells, 4,500; polymorphonuclear leukocytes, 61 per cent.; small lymphocytes, 34 per cent.; large lymphocytes,

3 per cent.; transitionals, 0; eosinophils, 1 per cent.; mast cells, 1 per cent. Two normoblasts and one megaloblast were seen. The red blood cells showed marked variation in size and shape. There were very many small cells but the majority were macrocytes and the average volume index was increased. There was no achromia and the color index was high. Occasional cells showed marked polychromatophilia and occasional cells showed very marked stipling.

Necropsy Protocol.—The body is that of a well developed, poorly nourished woman, 157 cm. in length. Rigor mortis is not present. No superficial lymph nodes are palpable. The skin is lemon yellow in color. The necropsy was performed thirty-six hours after death. The pupils are equal and regular and 0.4 cm. in diameter.

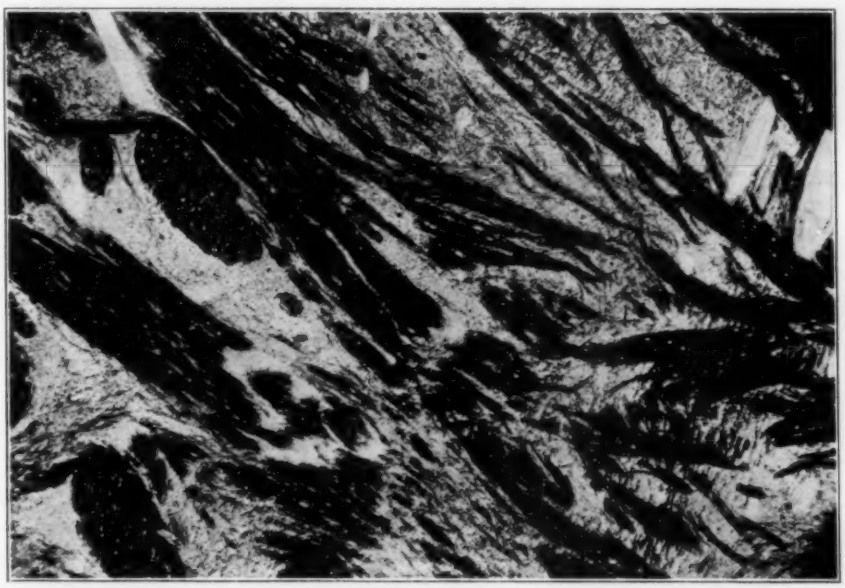

Fig. 10 (Case 2).—A section of the pons stained by Weigert's myelin sheath method. Here again are very clearly shown the miliary foci of Preobrajensky in the medullary substance.

Ventral Section: The abdominal fat is bright yellow; the thoracic and omental fat being bright lemon yellow. The liver is 12 cm. below the ensiform cartilage. The spleen is not encased in adhesions. The appendix is retrocecal and adherent to the cecum. The diaphragm arches to the lower border of the fourth rib on the right and to the lower border of the fifth rib on the left.

Heart: The myocardium of left ventricle shows tiger lily striations with here and there translucent areas. The muscle is soft.

Lungs: These are encased in adhesions. The cut surface is grayish brown in color at the apices. In the lower lobe it is pinkish-yellowish-gray. The connective tissue element is well marked. A frothy, grayish yellow, thick fluid is scraped from the cut surface.

Abdomen: The spleen weighs 185 gm. and is of firm consistency, with a shiny surface. It is purplish brown in color. The capsule is not thickened;

the trabeculae are prominent and the malpighian bodies appear as pin points.

Kidneys: These showed cystic areas on the lateral edge. The capsules stripped easily.

Liver: This weighs 1,560 gm. It is shiny, mottled and of yellowish-brown color. The capsule in general is not thickened. It is of firm consistency.

Pancreas: Pale; otherwise there is nothing of note.

Gastro-Intestinal: The stomach is pale, glassy and atrophic in appearance near the cardiac end.

Head: The skull tables show a symmetrical thickening. There are slight patches of endostosis in the frontal region.

Superior Surface of Brain: There is no apparent atrophy and it is firm to the touch. There are inequalities between the first and second frontals and between the right and left prefrontals.

Base of Brain: The basilar artery is small and no sclerosis in the circle of Willis could be seen. There is a slight thickening of the pia around the third nerves, otherwise the cranial nerves show no abnormalities. The mammillary bodies are flattened. The brain is pale. The fourth ventricle is clear. A pressure ring cerebellum is noted. In the left base the fluid is yellow. This also applies to the cortex. However, neither the right base nor the third ventricle showed this condition. The spinal fluid was mixed with blood. The brain weighed 1,175 gm., which according to Tigges' formula gives a loss in weight of 81 gm.

COLLOIDAL GOLD CHLORID REACTION

	1	2	3	4	5	6	7	8	9	10
Cortex	4	5	5	5	5	3	3	2	1	0
Left base	4	4	5	5	5	5	3	2	1	0
Right base	1	4	5	3	3	5	3	2	1	0
Third ventricle (blood stained)	0	0	1	1	2	3	3	2	1	0
Spinal fluid (blood stained)	0	0	1	4	5	5	3	3	3	2
Pericardial fluid	0	0	0	1	2	5	5	5	5	5

Histological Examination.—Weigert Section—Left Motor Area.—Small foci of degeneration resembling those described by Preobrajensky are noticed in the subcortical region. These, however, are not numerous. There are also some larger areas of degeneration that are in close relation to the blood vessels. The cortical perivascular lymph spaces are distended and here and there are associated with small areas of degeneration.

Pons: Here we also see miliary foci of Preobrajensky, but these, unlike those described in Case 1, are more numerous in the peripheral portions of the medullary substance. The myelin is thinned out in many places and in many instances this has gone on to complete degeneration. Three Lichtheim plaques were counted which were in intimate contact with the blood vessels. In addition, two sharply defined areas of degeneration, involving entire tracts, are present. These are also seen in the sections of the pons stained with cresylecht-violet and are more fully described under the latter heading. The gray matter showed practically no involvement.

Medulla: The white matter showed but slight involvement. Discretely scattered between the fibers of the raphe were small foci of degeneration. In the gray matter, however, it was not uncommon to come upon distinct areas of degeneration in the neighborhood of blood vessels. This was especially true of the dorsal portion of the medulla.

Cord: In the left lateral column of the cord, in the cervical region, there are several foci of the Lichtheim type. The blood vessels which are rather

Fig. 11 (Case 2).—Another section of the pons. Note the uneven demyelinization of an entire tract. The destruction has progressed very far in the center where large sclerotic areas have been formed. Compare this photograph with Figure 12 which is the same area stained with cresylecht-violet.

numerous have greatly thickened walls. In the lumbar region, there are patchy areas where the myelin is thinned out. The gray matter appears normal.

Cresylecht-Violet Sections—Left Motor Area.—The pyramidal cells, especially those in the outermost layer of the cortex, are shrunken and irregular in outline, the nucleus, in many cases, being crowded to one side. In others it is entirely absent. Satellite cells are numerous. Large stellate glia cells were observed. The blood vessels are numerous and the perivascular lymph spaces are uniformly distended. The subcortical area shows no large areas of degeneration but here and there a few small, clear areas.

Fig. 12 (Case 2).—Same area of pons as in Figure 11 stained with cresylecht-violet. This also shows the uneven degeneration of the entire tract. To its left, two other foci of degeneration are seen. (× 50)

Pons: Here we see many evidences of a pathologic process. In the medullary substance there are numerous sievelike areas. Here the destruction of the nerve fibers has not been accompanied by any considerable increase in the neuroglia fibers, thereby producing the cribriform appearance. One also notices large sclerotic areas which apparently are composed entirely of neuroglia. These hyaline-like areas involve entire tracts and are definitely circumscribed by fibers of other tracts which evidently have escaped being involved in the destructive process. Furthermore, these sclerotic areas are symmetrically distributed

on either side of the pons. In addition to the areas just described, there are numerous perivascular areas of degeneration. These vary in size and have no definite margins, but shade off insensibly into the surrounding tissue. One of these perivascular areas of degeneration extends into a small collection of nuclear cells which also show evidence of pathological involvement. They are irregular in outline. Many are shrunken and granular and some show a diffuse chromatolysis.

In the larger collections of gray matter, the perivascular spaces are distended and here and there one sees a patchy area of degeneration. These, however, are not numerous. The majority of the nerve cells show more or less changes. The axonal type of degeneration was observed.

Fig. 13 (Case 2).—Cresylecht-violet sections of the pons. Here there are two sievelike areas of degeneration surroundinng two blood vessels. This shows beautifully the intimate relationship between the blood vessels and the "anemic foci." Evidently in a given area, some of the nerve fibers succumb to the toxic action sooner than others. In this manner, no doubt, the cribriform or sievelike areas seen above are reproduced. (× 50.)

Medulla: In the white matter, there are streaky patches of degeneration. Vacuolization is pronounced. The pyramidal tracts show no changes. Very few of the nerve cells appear normal. The majority are highly granular and show more or less displacement of the nucleus. Clear areas, that appear like rifts in a cloud, are scattered about.

Cord: Many irregular, pale areas, containing necrotic tissue and surrounded by neuroglia, can be seen in the lateral columns. In some cases, the neuroglia

Fig. 14 (Case 2).—Another part of the same section. Here the degeneration, which surrounds the blood vessels, extends into a neighboring collection of nuclear cells. (× 50.)

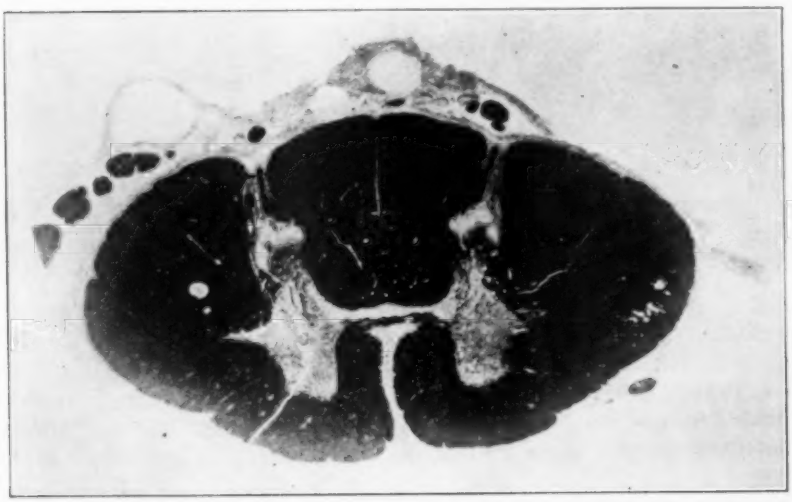

Fig. 15 (Case 2).—Weigert's myelin sheath stain. Section of the cervical region of the cord showing plaques of degeneration in the lateral columns. The hole in the right lateral column has been artificially produced to indicate the right side of cord. (× 10.)

cells seem to be clumped together. This is also met with but to a much lesser extent, in the posterior columns. The cells of the anterior horns are bizarre in shape and contain yellow pigment, similar to that described in the preceding case.

CASE 3 (Necropsy 18-34).—*History.**—J. H., a white boy, aged 6 years and 11½ months, was admitted to the Monson State Hospital, Jan. 15, 1917, with the diagnosis of epilepsy.

Family History.—Father and mother are living and well. The father was 36 and the mother 34 years old at the time of the birth of the patient. The patient is one of seven children. One older brother, who was an epileptic, died. There is no other history of insanity or feeblemindedness in the family. An older sister of the patient died of pneumonia, aged 2 months. Three older brothers are living and well. The oldest, however, had convulsions when teething at 1 year of age and had four convulsions during the following year. He was then circumcised and he has been free from convulsions ever since. Since the patient was born, one sister has died, aged 6 weeks, cause unknown. One younger brother is well.

Personal History.—The patient had a normal birth and infancy up to 2 years when he had his first convulsion. Teething was normal. He talked at 1 year and walked at 11 months. He has had no exanthemas, except chickenpox. He went to kindergarten and first grade, passed and got along as well as the other children.

Mental Condition.—Although the mother states that the patient went to kindergarten and passed the first year in graded school, he is defective in school knowledge of the first grade. He can count up to 100 but can write only the initials of his name. He can read and write no words at all. He reacts normally to the emotions and shows no other abnormal reactions except an apparent memory defect for daily occurrences. He behaves rather strangely at times, apparently not realizing just where he is going or what he is doing when out with other boys. He starts off aimlessly and apparently needs supervision. Binet tests, however, show his mental age to be 6.1 years. According to the Yerkes-Bridges scale he is 7.1 years mentally. His first seizure occurred at 2 years of age. According to the mother's statements, the patient was in a baby carriage which was being wheeled by a young girl when the carriage suddenly tipped over. The child was apparently unhurt. Eight hours later, however, he had a convulsion which the mother attributes to the fall. There is no history of unconsciousness or apparent injury at the time of the accident. Since that time, however, the patient has had seizures, both of grand mal and petit mal type. These, furthermore, have been increasing in frequency of late and at present occur almost daily.

Physical Examination.—The patient shows no marked asymmetry. Head measurements: circumference, 20 inches; glabella to inion, 11 inches; transverse, 10 inches. The neurological examination showed nothing abnormal. The blood Wassermann reaction was negative.

Course.—The patient remained at the hospital until June 27, 1916, and during that time had on an average ten convulsions per month. He gained in weight and height, but had made little or no progress in school. He had an attack of status epilepticus of twenty-six grand mal seizures. He was readmitted to the hospital on Oct. 20, 1917, without any apparent change in his physical condition. He had had an attack of status epilepticus while home on

* This case will be reported more fully in a later paper.

a visit. A second Wassermann test was reported negative. After readmission he had less seizures, averaging only two or three each month, but he exhibited a marked change in his mentality. He attended school but without making any progress. At times he would play and associate with other children, sing songs which he had committed to memory and appear quite normal. At other times, lasting for periods which varied from a few hours to several days, he would be very seclusive; hide himself about the ward, in closets, under beds; would not associate with the other children, but would be found sitting alone quietly and if asked the reason for so doing would reply, "Other boys are rough and intend to kill me." Very often he would volunteer the information that he was going to kill himself but would not specify in what manner.

There was no marked change physically or mentally until April 16, 1918, when the patient was noticed to be suddenly acutely ill. He vomited several times, complained of headache, and there was a slight rise in temperature.

Fig. 16 (Case 3).—Section of the left motor area showing numerous foci of degeneration which vary greatly in size. Weigert's myelin sheath stain.

By the 21st the condition had somewhat improved. There was no nausea or vomiting and the patient took liquid nourishment fairly well. The skin of the whole body had a marked greenish, lemon yellow tint. The mucous membranes showed marked pallor. A blood examination showed hemoglobin, 70 per cent.; 70,000 leukocytes and 2,000,000 red blood cells. The color index was high, namely, 1.75. A differential count gave polymorphonuclear leukocytes, 57 per cent.; small lymphocytes, 20 per cent.; large lymphocytes, 21 per cent.; transitionals, 1 per cent.; basophils, 1 per cent. A differential stain showed granular degeneration of the red cells, presence of nucleated reds, and also some megaloblasts.

In the night the patient was very restless and exhibited a marked psychosis. With his finger nails he tore a gash in the perineum, anterior to and extending into the rectum. He also scratched his face and hands with his finger nails

On the 24th he was more quiet but still threatened to destroy himself and had to be restrained. The skin still retained the same peculiar hue and there

were no different physical signs. Toward evening the temperature rose to 103 F., and early the next morning the patient died.

Cause of Death: Pernicious anemia.

Necropsy Protocol.—Necropsy was performed ten hours after death. External Examination:—The body is that of a slenderly built, poorly nourished, white male child, 9 years of age. The skin has a bluish gray appearance over the abdomen and lower chest, with yellowish cast of all muscle depressions over the chest and neck. There is a faint yellowish tinge to the sclerae. The submaxillary glands are prominent. The lymph nodes posterior to the sternocleidomastoid as well as the axillary and inguinal glands are palpable. The pupils are unequal, the right being 2 mm. and the left 4 mm. in diameter. The teeth are also unequal in size. Rigor mortis is present. The body length is 127 cm.

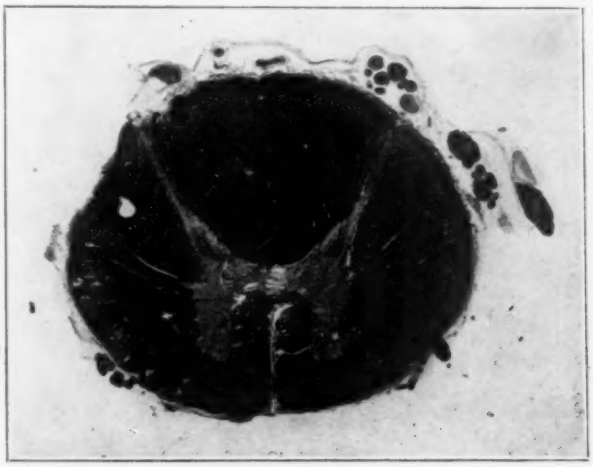

Fig. 17 (Case 3).—Section of the dorsal region of the spinal cord. The right lateral column is principally involved. Some degeneration changes have also occurred in the anterior columns. (× 10.)

Ventral Section: The fat over the abdomen is of a pale lemon color and moist. The muscles are red. The lower border of the liver is 5 cm. below the ensiform cartilage. It is brown in color. The spleen is large and free. The appendix is also free and measures 8 cm. in length. The mesenteric lymph nodes are enlarged and some are calcareous. The diaphragm arches to the third interspace on the right and to the fourth interspace on the left.

Heart: The heart muscle is firm, grayish pink in color and shows no white areas or fat.

Lungs: Both lungs showed slight congestion in the posterior portions of the lower lobes.

Organs of the Neck: The thymus is present. The tissue is stringy, but very little of the gland tissue is left.

Abdomen: The spleen shows three fetal lobulations. The pulp is firm and the malpighian bodies numerous. The kidneys show nothing abnormal. The liver weighs 1,240 gm., and a cut section looks greenish yellow. It is homogeneous, there being very scant outlining of the lobules.

Gastro-Intestinal: There were depressions in the gastric mucosae suggesting beginning ulcerations.

Head: The skull is pale in color and shows irregular thinning over the vortex and frontal region.

Brain: The dura is adherent to the calvarium. The cortex shines through a thin and delicate pia mater which is gray. The cranial nerves appear smaller than usual. The frontal lobes appear out of proportion to the parietal. The temporal tips are unequal in pattern, the left being more complex than the right. The hemispheres of the cerebellum are also slightly unequal, the left being the larger. The brain substance is firm, especially the right frontal region. The weight of the brain is 1,280 gm., which represents a gain of 264 gm., according to Tigges' formula.

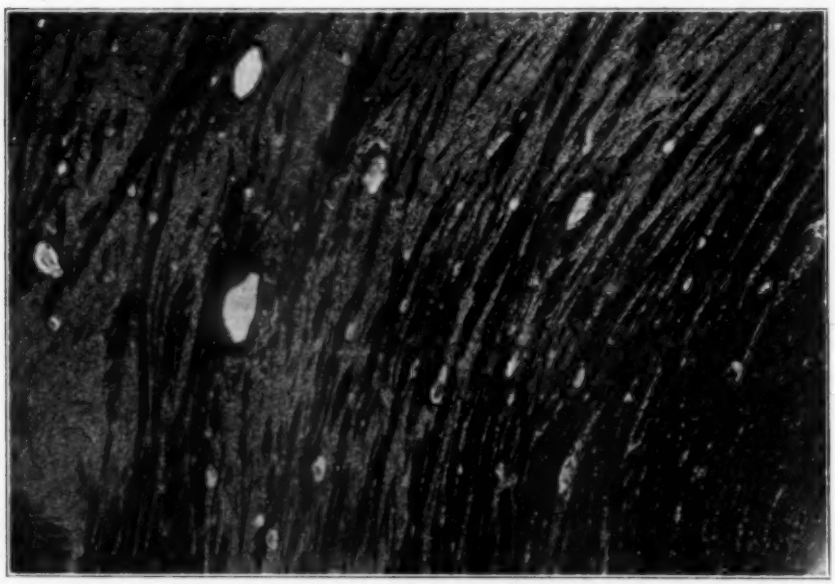

Fig. 18 (Case 3).—Just as in the two preceding cases, this section of the pons also shows the miliary foci of Preobrajensky. Weigert's myelin sheath stain.

Cord: The cord shows "china white" softening in the posterior columns, especially in the lumbar region.

Histological Examination.—Weigert Sections—Left Motor Area: In the subcortical areas, the perivascular lymph spaces are distended and clear. Many small discrete foci of degeneration and four larger sclerotic plaques were noted. The cortex itself does not present anything unusual.

Pons: This section, like the two preceding sections of the pons, also contains the miliary foci of Preobrajensky. However, they were not nearly as numerous nor as universally distributed, being limited to a small portion of the medullary substance. The blood vessels in the nuclear masses are thickened and filled with red blood cells. The perivascular spaces are markedly distended, and some also contain red blood corpuscles.

Medulla: Here there is only slight evidence of pathological involvement. The lesions found are similar to those described above.

Cord: (*Cervical region*).—In the lateral column, near the anterior horn, there is a well-defined focus of degeneration of the Lichtheim type. The lateral cerebellar tracts show patchy myelin sheath degeneration, with here and there evidence of vacuolization. (*Dorsal region*).—Here the lesions are even more marked. The anterolateral columns show great involvement. Many foci of degeneration, including a Lichtheim focus, are seen. The blood vessels do not show any abnormalities. (*Lumbar region*).—This section shows nothing of note.

Cresylecht-Violet Sections—Left Motor Area.—The principal abnormality noted was on the part of the pyramidal cells. A large number of these cells were shrunken and the contour of their nuclei was not clear cut. Some were highly granular and some were surrounded by satellite cells. Here and there in the subcortical area there were small vacuoles.

Pons: Here the changes in the nerve cells are similar to those just described, only much more accentuated. The axonal type of degeneration was observed. The larger pyramidal cells did not appear to be as greatly involved as the smaller.

Medulla: Here one notices large sclerotic areas which are apparently closely identified with the blood vessels. Small, clear, hyaline-like areas are fairly numerous. The nerve cells show but insignificant changes.

Cord: (*Cervical region*).—The blood vessels are slightly thickened and the perivascular spaces are distended and filled with hyaline-like material. (*Dorsal region*).—Here we meet with ballooning of the nerve fibers with the formation of clear sievelike spaces. There does not appear to be an increase in the neuroglia. Many of these irregular areas are in close proximity and even surround the blood vessels. The cells in the anterior horns show a high degree of chromatolysis. Some of the cells appear to be entirely disintegrated. (*Lumbar region*).—In this region there is very little of a pathological nature to be seen.

Case 4.—(Necropsy 16-52.—*History.*—J. F., aged 53, was committed to the Northampton State Hospital for the Insane, May 10, 1915. The medical certificate reads as follows: "Patient is recovering from an acute exacerbation of a chronic nephritis. Patient has a cross on his arm, which he hopes will prove certain things if he can see the priest. Wishes to see the selectmen about certain property and wishes to tell them that while there is life there is hope; that the sky is blue and other such things. Wishes to see a lawyer about disposing of his property. Is an inmate of almshouse and has none."

General Appearance.—The patient is a well-nourished, simple looking man, over 50 years of age, very anemic in appearnce. During the examination he was quiet, but listless and indifferent. He did not volunteer conversation, replying correctly, however, when directly questioned. There was no stereotypy, autonomy, blocking or flight of ideas, or other abnormalities noticeable, except possibly a slight retardation. This may be his normal reaction, as he does not appear overbright.

Family History.—His father is said to have been insane. One brother is in Baldwinville (hospital for chronic infantile neurological cases), and another brother was in the Northampton State Hospital, the diagnosis in his case being manic depressive insanity.

Personal History.—The patient was born and brought up in Ware, Mass., where he spent all of his life except for short occasional absences. He can only read and write. He was never employed except as a common laborer. He

worked, however, only intermittently, and for the greater part of his life was looked after by his sister. For the past several years he has been in poor physical health. He cannot state anything exact concerning this, but says that his appetite has been poor and that he believes he has kidney trouble. At one time he is said to have been very intemperate, but denies drinking to any extent for several years prior to his admission to the hospital. In 1910, he was committed to the Howard (R. I.) State Hospital. The diagnosis at that time was delirium tremens. Three years later he was again admitted to the Howard State Hospital, where a provisional diagnosis of chronic alcoholism was made. The mental examination at that time, showed depression and

Fig. 19 (Case 4).—Numerous areas of degeneration of varying sizes are shown in this picture of the cortex. In several, the close relationship to the blood vessels is seen. Weigert's myelin sheath stain.

defective knowledge of current events. The patient denied hallucinations, but it was stated that a short time before coming to the hospital he heard noises on waking from sleep. He was discharged in 1914 and returned to his home from where he was sent to the Ware Almshouse. From there he was committed to the Northampton State Hospital.

Physical Examination.—A summary of the physical examination reads as follows: "Fairly well nourished male with rather poor muscular development and of decidedly anemic appearance. The mucous membranes are very pale. There is a complaint of dyspnea on exertion and of discomfort after eating. Appears very much like pernicious anemia."

Neurological Examination.—There are no unusual phenomena observed. The patient is quiet on examination. All motions are slow and deliberate. There is no tremor or flush.

Muscle Power: This is poor.

Coordination: There is a slight swaying in the Romberg position, but he is able to stand without support. The gait is normal. Coordination tests were fairly well, although slowly performed.

Fig. 20 (Case 4).—Weigert section of the pons. In this photograph, the Lichtheim type of focus predominates. A few of the miliary foci of Preobrajensky are also present. Note the distention of the perivascular spaces.

Sensation: The feet and hands are slightly cooler than the other portions of the body. Stereognostic sense is normal.

Cranial Nerves: The pupils are normal in size and equal and react to light and accommodation. All the other cranial nerves are normal.

Reflexes: The superficial reflexes are entirely absent. The knee jerks are absent. The other tendon reflexes are very faint. There are no abnormal reflexes.

Mental Examination.—Orientation: Good in all spheres. Memory: Remote and recent memory rather poor. He remembers things in general ways but cannot give details nor dates, and appears somewhat demented.

Education: He is very poorly educated. He can read and write, but has little general knowledge, and no knowledge at all of current events.

Delusions: On admission, he talked of vague unsystematized, indefinite delusions of owning considerable property which was due him from his father's estate. Mild delusions of persecution against his sister were also present, he believing that she had deprived him of his share of the estate. He made other vague statements, but his whole delusional formation was very loosely connected. He talked only when directly questioned and gave the impression of being considerably deteriorated.

Fig. 21 (Case 4).—Section of the cervical region of the spinal cord. The posterior and postero-lateral columns are involved. A narrow strip on either side of the posterior fissure has escaped involvement in the pathologic process. Weigert's myelin sheath stain. (× 10.)

Hallucinations: No definite hallucinations could be elicited. The abstract from the hospital at Howard, R. I., states that before his admission there he was hearing noises on waking from sleep. This may possibly have been a mild hallucinosis following drink.

Emotional Tone: He takes very little interest in anything about him. He shows neither exhileration nor depression, but always appears indifferent.

Demeanor: Since his admission he has been quiet and fairly cheerful. He never volunteers conversation with any one but answers when directly questioned.

Attention: This is fair.

Abstract of Ward Notes.—On admission, he was correctly oriented. He remembered that his brother had once been a patient at the hospital. The

patient complained of not feeling well physically. He believed he had kidney trouble. He talked vaguely of his delusions and denied that he had been intemperate in recent years. He was quiet and conducted himself well. At first he helped a little in the ward when requested, but made no attempt to associate with any one, although he could not be considered surly. When

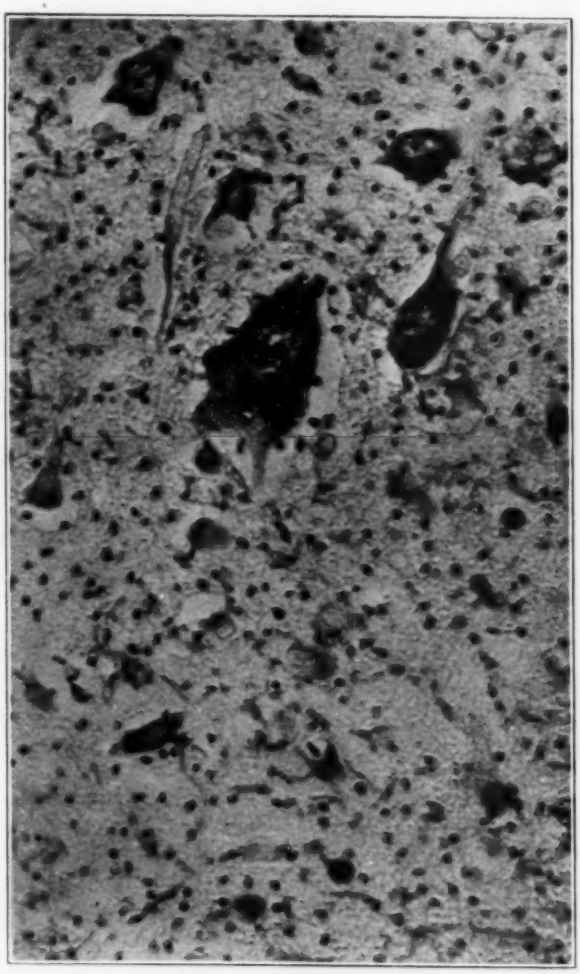

Fig. 22 (Case 4).—This is a section of the cortex stained with cresylecht-violet. A large pryramidal cell (neuronophage) can be seen which is evidently greatly swollen and undergoing degeneration. It contains two glia cells, one being within the cell body and the other within the nucleus in close contact with the nucleolus. (× 100.)

addressed, he would reply but would not continue the conversation. He took no interest in games, in reading or in the discussion of his fellow patients. Whether this listlessness was due to deterioration or to his poor physical condition was difficult to determine.

In June, 1915, he began to complain of epigastric pain and of a feeling of heaviness following the taking of food. In September, a slight dyspnea was noticed on exertion and the epigastric distress had become so marked that he could only take malted milk, vomiting every other food. The skin showed the peculiar brown tinge peculiar to pernicious anemia. A single blood count showed 3,260,000 red blood cells and a hemoglobin of 60 per cent. Numerous poikilocytes, microcytes, and macrocytes were seen, but no nucleated reds were seen at this time. There was puffiness about the eyes. Some days he complained of weakness in the legs.

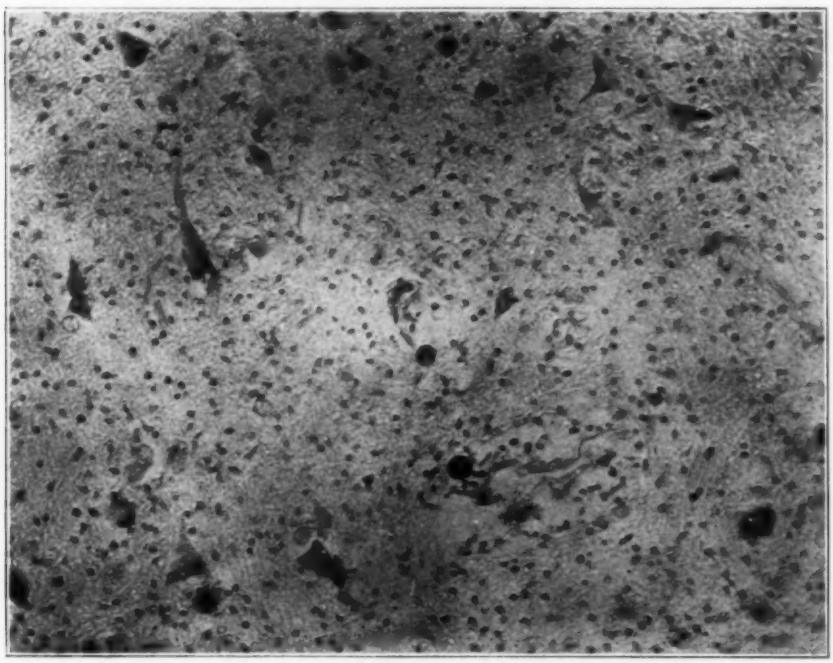

Fig. 23 (Case 4).—Another view of the cortical motor area showing disintegration of the pyramidal cells, and distention of the pericellular spaces. Some of these cells are pale, shrunken, irregular in outline, stain poorly and unevenly, and show eccentricity of the nucleus. The severe neurogliar reaction is evident. In the lower right hand corner of the field, note the large sclerotic area surrounding a blood vessel. Cresylecht-violet stain. (× 50.)

In October, physical failure became more marked. The dyspnea was so intense that care in bed became necessary. Puffiness of the eyes, hands, and feet was very noticeable. Mentally he was very dull, apparently comprehending but little. In November, 1915, a note in the history was made that he seemed slightly improved, which temporary improvement continued until April, 1916. In January, 1916, typical findings of pernicious anemia were present in the blood and especially the nucleated red blood cells. Early in April he failed rapidly and died on April 15, without showing any new development of his disease.

Necropsy.—Protocol (16-52).—Necropsy was performed two hours after death. The body is that of a white male, 168 cm. in length. The skin is pale

lemon yellow, especially over cheeks, forehead, and arms and legs. There is considerable pigmentation over the back, chest, face and lower abdomen. Rigor mortis is present in jaws and legs. The lymph nodes are not palpable. The pupils are equal and measure 0.4 cm. in diameter. The eyeballs are slightly softened. The teeth show Riggs' disease.

Ventral Section: The fat over the abdomen is pale yellow and moist. The muscles are red and mixed with apparent fatty streaks. The lower border of the liver is 1 cm. below the ensiform cartilage. There is a slight amount of free fluid in the flanks. The appendix is 8 cm. in length. The tissue in the pelvis appears bloodless. The spleen is surrounded by adhesions. The diaphragm arches to the third rib.

Thorax: The sternal marrow is richly red and somewhat fluid. There is a free fluid in the left chest and the pericardial sac is thickened.

Heart: The epicardial fat is abundant and there are milk spots on the posterior surface. The heart muscle shows white mottling and also minute hemorrhages in the right auricle. It fragments easily.

Lungs: They show very little of note.

Abdomen: The spleen is grayish red and its capsule is slightly withered. A section shows the pulp to be red. It measures 10 by 5 by 2 cm.

Adrenals: These are small and softened.

Kidneys: There is an excessive amount of fat around the kidneys which are yellowish brown in color. The pyramids are white and poorly differentiated from the surrounding tissue. Two cysts containing fluid are seen.

Liver: There are slight irregularities over the surface of the liver which is yellowish red in color. A section shows packing together of the lobules. It measures 23 by 16 by 7 cm.

Pancreas: This organ is dotted with hemorrhages.

Gastro-Intestinal: The stomach is large and contains some fluid. The mucous membrane of the stomach is shiny.

Brain: The dura shows signs of absorption in the frontal region and of thickening along the longitudinal sinus. A slight amount of yellow fluid escapes on section of the dura. Points of hemorrhages are seen in the pia mater which shows some thickening along the vessels. It is held up from the cortex by fluid in the motor regions. The brain appears yellowish white. The right lobe sags, being apparently slightly shorter than the left. The pattern of convolutions is more nearly circular over the right lobe than over the left lobe. The brain has a resilient feeling. From the basal aspect, it is noticed that the pia is thickened over the pons, left third nerve, and optic chiasm. The left temporal tip is softer than the right. The left cerebral artery is larger than the right. The fourth ventricle is clear.

COLLOIDAL GOLD REACTION

	1	2	3	4	5	6	7	8	9	10
Right base	0	0	0	1	2	1	0	0	0	0
Left base	0	0	0	1	1	1	0	0	0	0
Third ventricle*	0	0	0	0	0	0	0	0	0	0
Spinal fluid	0	0	0	0	0	0	0	0	0	0
Pericardial fluid	0	0	0	0	0	0	0	0	0	0

* Slightly bloody.

Histological Examination.—Weigert Section—Left Motor Area.—The medullary substance shows little of note. There are a few areas where the myelin has been completely destroyed and also a few places where there is a thinning out of the myelin.

Paralleling the edge of the cortex, there is a narrow strip of tissue which stains less heavily than the surrounding tissue. Under high power, this area is shown to contain small irregular shaped spaces which for the most part are structureless. A few are crossed by undegenerated or only partially degenerated nerve fibers. In this area, furthermore, the capillaries are very numerous and the perivascular spaces are distended.

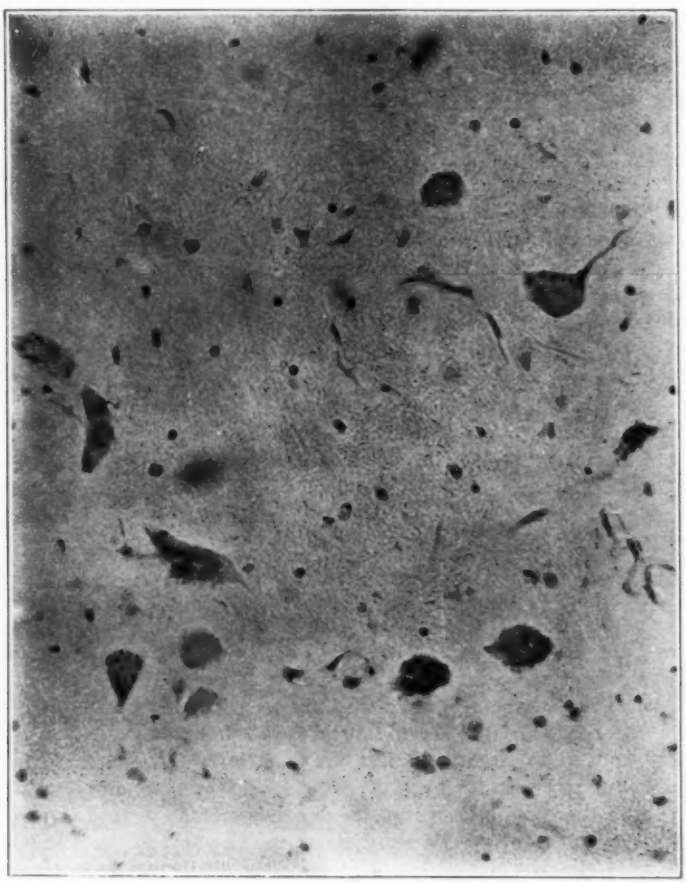

Fig. 24 (Case 1).—Section of cervical region of spinal cord stained with cresylecht-violet showing some anterior horn cells containing yellow pigment. This pigment is diffuse, slightly granular, and occupies the central portion of the cell body, the protoplasmic substance being pushed to the extreme periphery. The two cells in the lower left hand corner of the field are practically nothing but a mass of pigment. (× 100.)

Pons: Here we see large foci of destroyed tissue in intimate relation with the blood vessels. It is almost possible to trace the entire process of their formation as they are present in all stages of development. One notices first a slight thinning out of the myelin sheaths in the immediate neighborhood of a blood vessel. The process continues and this thinned out area becomes

sievelike, due to the lack of uniformity in the destruction of the myelin sheaths. In the meshes of some of these cribriform areas, red blood cells are found. In the more advanced places, there has been an increase in the neuroglia with resultant formation of large plaques of sclerotic tissue. In one part of the field, the miliary foci described by Preobrajensky were also observed.

Medulla: Small ragged foci of destroyed tissue, irregularly distributed are seen. The perivascular spaces of the blood vessels in the olivary nuclei are markedly distended.

Cord: (*Cervical region*).—In this region, there are numerous small foci where the myelin sheaths have been destroyed with subsequent vacuolization. This destructive process has occurred principally in the columns of Burdach. The columns of Goll are but slightly affected. The direct pyramidal tracts show more or less degenerative changes also. (*Dorsal region*).—This region appears practically normal. In the gray matter of the anterior horns one can see several small hemorrhagic areas. This is also present in the lumbar region which otherwise shows nothing of note.

Cresylecht-Violet Sections.—Left Motor Area.—The cortical region shows extensive pathologic involvement. There is a tremendous overgrowth of neuroglia both of the fibers and cells. The latter are encroachinng on the pyramidal cells. The glia cells are of two kinds: (1) a small and apparently homogeneous cell, and (2) a large cell with a granular nucleus which in many ways resembles a small lymphocyte. In several instances, these cells both large and small are seen to be incorporated in the body of the pyramidal cells and in one instance one of these larger cells is seen to be incorporated within the nucleus of the nerve cell. The nerve cells, with but few exceptions, show marked degenerative changes. They are shrunken, irregular in outline, and the protoplasm is not uniform in structure. The nuclei show chromatolysis and their outline is hazy. Their position varies, being either to one side or at the end of the cell. Some of the cells instead of being shrunken are tremendously swollen. In some cases, the nerve cell seems to have disappeared entirely or fallen out, the pericellular spaces being occupied by glia cells.

The blood vessels also show a severe reaction. The perivascular spaces are distended. The capillaries show a tremendous increase. One sees them in all stages of development, from the small, budding, rod-like projection to the thin-walled vessel with an almost imperceptible lumen.

All these pathologic changes gradually decrease in intensity as we approach the subcortical area. In the latter structure, there are many clear areas in which no nerve fibers are seen. These areas are irregular in size and shape In the larger ones, glia fibers have replaced the nerve fibers, giving the area a hyaline-like appearance. This is brought out very distinctly with the eosin-methylene blue stain.

Right Peduncle: There is a uniform distention of the perivascular spaces, many of which are contiguous to foci of degeneration. Some of these areas are cribriform or sievelike in appearance. The pyramidal cells show evidence of involvement. Some are completely disintegrated, some have lost their nuclei and are highly granular, and others are pigmented. Satellitosis is marked.

Pons: Small, clear, fairly regular areas corresponding, in all probability, to the miliary foci of Preobrajensky that were seen in the Weigert Section, are present in the raphe. The nerve cells do not show as great an involvement as those in the preceding sections. Only a comparative few are entirely disintegrated and none show pigmentation. The perivascular spaces are distended. There are also patches of neuroglia overgrowth.

Medulla: The nerve cells in the different collections of gray matter show uniform degeneration of varying intensity. The pericellular spaces are enlarged. Pigmentation occurs frequently. Some of the blood vessels show a thickening of the intima and a small number are surrounded by small areas of degeneration.

Cord: (*Cervical region*).—There is a sharply defined sclerotic area in the posterior column which is identical with that seen in the Weigert Section. This area is composed chiefly of massive wavy bundles of neuroglia fibers with which are intermingled an occasional undegenerated or only partially degenerated nerve fibril. The nerve cells in the posterior horns appear shrunken in size and the nuclei do not stain well. The anterior horn cells show some pigmentation. This is especially true of those in the lumbar region. The character and location of this pigment are different from that of the pigment normally present in the cells of people 50 years or older. In this case, the pigment is granular, and diffusely and evenly distributed over the central portion of the cell.

DISCUSSION

A brief résumé, contrasting the clinical with the pathologic findings reveals a fairly uniform and definite relationship. In Case 1, we can assume from the history that the condition had probably existed for about three years although a blood examination was made only five days before death. On the clinical side we find a typical blood picture of pernicious anemia; absence of all the superficial reflexes with the exception of the left inguinal reflex; absence of both patellar reflexes and sensory disturbances in the form of numbness of the feet. Mentally, the patient had visual hallucinations, paranoid ideas and mild delusions of persecution. The necropsy report showed the characteristic changes on the part of the heart and stomach. Contrasted to this clinical picture there are definite pathologic findings. In the motor area we find characteristic vascular changes, pyramidal cell changes, satellitosis, vacuolization and the presence of the Lichtheim foci of degeneration. In the pons we have in addition to the above changes the miliary foci of Preobrajensky. In the spinal cord, the posterior column is practically entirely destroyed especially in the cervical region. Neural and vascular changes are also present. Pigmentation of the cells is pronounced and the neuroglia changes marked.

In Case 2 there is a definite blood picture of pernicious anemia. From the history we can safely infer that the condition had existed for many years. Clinically, there are neurological disturbances in the form of hyperesthesia of the lower extremities and an unsteady gait and mental symptoms similar to Case 1, namely: visual hallucinations, delusions of persecution, and paranoid ideas. The necropsy examination revealed a pale, glassy atrophic stomach and a heart with tiger-lily striations. Histologically, the cortex showed areas of degeneration

with vacuole formation, vascular changes, pyramidal cell changes, satellitosis and a marked increase in the neurogliar elements. The pathology of the pons was practically the same as that of the cortex, but again with the addition of the miliary foci of Preobrajensky. The spinal cord presented practically the same pathologic picture as the first case.

In Case 3 the clinical picture is somewhat different. In the first place the patient was very young, being about 9 years old at the time of his death; in the second place he was a decided epileptic, and in the third place the onset of the pernicious anemia was acute. Hence, clinically, we have comparatively few findings. There were no neurological changes, but mentally he showed delusions of persecution and paranoid ideas. During the height of the fatal attack, he showed a marked psychosis. On necropsy, there were slight changes in the stomach, resembling beginning minute ulcerations. The heart was negative. The brain showed a gain in weight, according to Tigges' formula. of 264 gm. However, Tigges' formula is not strictly applicable to children. Pathologically, in the cortex, the changes were similar to those in the first case except that they were less marked. No neurogliar changes were seen which was to be expected, considering the short duration of the disease. On the whole, the changes in this case were the least marked. Here again, however, the miliary foci of Preobrajensky were found in the pons.

In Case 4 the process evidently had gone on for several years. The blood picture was typical. There were marked neurological disturbances, all the superficial reflexes and both knee jerks being absent. There was also a distinct weakness of the legs. Mentally, there were paranoid ideas and delusions of persecution and other vague unsystematized delusions. No definite hallucinations were elicited. On necropsy the heart showed milk spots, white mottling, and minute hemorrhages. The mucous membrane of the stomach was shiny. The histopathologic changes were similar to those in Case 2. No Lichtheim focus was seen in the cortex. There was a marked increase in the neurogliar elements. Neuronophagic action of the cells was marked. The pons showed the miliary foci of Preobrajensky, the Lichteim foci, vascular changes and slight nerve cell changes. In the spinal cord, the columns of Burdach showed the greatest involvement. The nerve cell changes were slight. Pigmentation was present. Also vascular changes. There was a considerable increase in the neuroglia.

The following tables show these results in tabular form:

TABLE 1.—Summary of Clinical Findings in the Cases Reported

	Case 1	Case 2	Case 3	Case 4
1. Duration:				
(a) From symptomatic standpoint	3 years	Many years	Acute	Several
(b) Laboratory standpaint	5 days	1 year	Acute	1 year
2. Blood picture	+	+	+	+
3. Neurologic Findings:				
(a) Pupils	Normal	Sluggish	Normal	Normal
(b) Superficial reflexes	All absent except left inguinal	Not stated	Normal	Absent
(c) Knee jerks	Absent	Sluggish	Normal	Absent
(d) Abnormal reflexes	None	None	None	None
(e) Sensory disturbances	Numbness of feet	Hyperesthesia of lower extremities; unsteady gait	None	Weakness of legs
4. Mental Findings:				
(a) Hallucinations (visual)	+	+	None	Doubtful
(b) Delusions of persecution	+	+	+	+
(c) Paranoid ideas	+	+	+	+
5. Necropsy Findings:				
(a) Skin	Lemon yellow	Lemon yellow	Yellowish	Lemon yellow
(b) Fat	Lemon yellow	Lemon yellow	Lemon color	Pale yellow
(c) Marrow: (a) Sternum	Yel. pink	Not given	Not given	Richly red
(b) Femur	Raspberry red			
(d) Heart	Enlarged white striation	Tiger lily striation; no enlargement	Normal	No enlargement, milk spots, white mottling; hemorrhages
(e) Spleen	165 grams	185 grams	160 grams	13.5 × 10 × 1.5 cm.
(f) Liver	1,800 grams	1,560 grams	1,240 grams	23×16×7 cm.
(g) Stomach	Thick walls; glossy; no rugae	Pale, glossy, atrophic	Ulcerations?	Mucous membrane shiny
(h) Brain	Loss 308 grams	Loss 81 grams	Gain 264 grams	Not given
(i) Cord	Minute specks of translucency in posterior columns	Not stated	China white softening in posterior columns	Not stated

TABLE 2.—Summary of Histologic Findings in the Series of Cases Reported

	Case 1	Case 2	Case 3	Case 4
1. Motor Area:				
(a) Vascular changes	+	+	+	+
(b) Lichtheim foci	+	Not definite	None	None
(c) Vacuoles	+	+	+	+
(d) Pyramidal cell changes	+	+	+	+
(e) Satellitosis	+	+	+	+
(f) Neuroglia changes	Slight	Marked	None	Marked
2. Pons:				
(a) Miliary foci of Preobrajensky	+	+	+	+
(b) Lichtheim plaques	+	+	None	+
(c) Nerve cell changes	Not marked	+	+	Slight
(d) Vascular changes	+	+	+	+
3. Spinal Cord:				
(a) Posterior column degeneration	++	Very slight	+	+
(b) Lateral column degeneration	+	+	+	Slight
(c) Vascular changes	+	+	+	+
(d) Nerve cell changes	+	+	+	Slight
(e) Pigmentation	+	+	None	+
(f) Neuroglia changes	Marked	+	None	+

From the above tables, it is evident that the neuropathology of the brain in pernicious anemia is larger and more fruitful than that of the cord. It is true, of course, that all these cases showed very definite mental symptoms and hence one would naturally expect to find cortical

changes. However, in the case of J. H. (Case 3) who had a definite psychosis with no neurological disturbances, the cord changes were by far more marked and had progressed much farther than the cortical changes. From this one might argue that in pernicious anemia, the first degenerative changes occur in the cord; then the process gradually extends and involves the brain.

In the third case, there was also very little involvement of the neuroglia. This, as well as all the other points in which this case differed from the others, can be readily explained on the ground that this case had an acute onset and ran a very rapid course.

The significance of the presence of the miliary foci of Preobrajensky in every section of the pons is open to speculation. Are these lesions specific for pernicious anemia or is their uniform presence in the pons merely a coincidence? Obviously, one should not generalize from the findings of only four cases. However, to look on the regularity of their presence as merely a coincidence seems to me to be unjustifiable. At any rate, it is a point worthy of note and of further investigation.

CONCLUSIONS

1. There appears to be a fairly definite and constant relationship between the clinical symptoms and the pathologic changes.

2. The psychoses can be classified with the symptomatic psychoses of a toxic-organic nature. The whole delusional formation is vague, unsystematized and loosely connected.*

3. The brain changes are even more marked than the cord changes provided the disease has existed for a considerable length of time. This, in my opinion is due to the fact that in addition to the toxic action of the poison on the pyramidal cells, metabolic changes also occur in the nerve cells as a direct result of the long standing anemia.

4. The blood vessels, pyramidal cells and the medullary fiber show similar degenerative changes at different levels of the central nervous system.

5. The foci of degeneration bear a definite and distinct relationship to the blood vessels.

6. In every case, the miliary foci of Preobrajensky were found in the pons.

7. Some of the nerve cells in every case with the exception of the third case, which was of very short duration, show diffuse pigmentation.

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* It is quite possible that further investigation will prove that these psychoses are due to an encephalitis, and that therefore they belong in the group of encephalopsychoses rather than in the group of somatopsychoses.

8. In speaking of the neuropathology of pernicious anemia, it is not sufficient merely to describe the lesions found in the spinal cord. The brain changes are too numerous and definite to be omitted. The neuropathology of pernicious anemia should include the entire central nervous system.

I wish to express my thanks to Dr. Elmer E. Southard not only for placing the clinical material at my disposal, but also for his many helpful suggestions in carrying out this study. I also wish to thank Dr. M. M. Canavan for her kindly interest and capable supervision. These have been of inestimable value to me in the preparation of this paper. My thanks are also due to Miss E. R. Scott for her care in the preparation of the sections, and to Mr. H. W. Taylor for his care in the preparation of the photographs.

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Abstracts from Current Literature

L'HYSTERIE CHEZ LES PRISONNIERS DE GUERRE INTERNES EN SUISSE. A. Repond, Schweiz. Arch. f. Neurol. u. Psychiat. **3**: 128, 1918.

An interesting point is contained in this article by an observer, apparently so placed as to have surveyed mental reactions under conditions that might specify further our notions of the psychogenesis of hysteria. He states that the Belgian and French prisoners of war, interned in Switzerland, have presented more frequently striking forms of hysteria, than have prisoners of these countries while held in German camps, quoting here from Birnbaum's articles.

The attacks were of the classic convulsive type with rigidities, excitement and amnesia. A considerable hysterical background was revealed in most by their impulsiveness, lability, suggestibility, hypochondrical notions, profound egocentricism and in many a pseudologia-fantastica. No traumatic causes could be isolated. As precipitating factors he saw the refusal of privileges, delays of letters, imposition of hard work, unsuccessful attempts at repatriation.

It may be that what is sifted down in the subjects of these observations are those definite hysterical types presenting in any given mass. What arrests the attention is the higher percentage of obvious hysterical disorders here than obtain in the camps of Germany. We are familiar with the type of conflict, defined by MacCurdy in the "Neuroses of War," as the most effective precipitator of the hysterical reactions; in these concepts the notion of the herd being given a nuclear position rather than the unconscious bases of the usual type.

The psychic factors contained in an internment camp are of course not strictly comparable to those with which MacCurdy had to do, for there is an apparent termination here of the immediate hazard of battle. From the Teutonic sources gathered by our author this is borne out in the relatively lesser number of the hysterical manifestations occurring there. Yet in the Swiss camp, where the step to freedom has been made, where repatriation is more nearly possible, the hysteria appears in its massive form. It looks as though the mechanism or the wish shrewdly has bent to the rigid and harsh reality of a German prison camp; but where the wish approaches as possible of fulfilment, at a site where repatriation may be gained, there is put under way in its most infantile and regressive form all the underlying movement of the unconscious.

The wishes sought to be gained are, however, not simply those involved in the freedom of the individual, but are discovered, for example, in a desire for the better quarters of the hospital, to which a malady may assign them, or to gain funds, or special attention. They appear frequently as threats to the officer if he failed to grant the privilege sought. Nor is the percentage of cure found here at all comparable to that which obtains at the front. The psychotherapeusis which succeeds best is one containing a promise of immediate advantage in case the malady immediately terminates. Those are cured who wish to remain cured.

One gets an illumination here of the value of the reality principle in the hands of those treating the neuroses at the front and assures one that beneath those conflicts whose solutions there have been so readily gained, there may remain concealed a characteristic infantilism to which under certain conditions the psychoneurotic appears always to regress.

PARKER, New York.

WHAT THE WAR HAS TAUGHT US ABOUT TETANUS. LOUIS BAZY, M.D., Lancet, **2**:523 (Oct. 19) 1918.

As preventative, antitetanic serum has proved itself of very great value and the systematic administration of antiserum has proved wise. However, cases of tetanus have developed in spite of serum either (*a*) because the serum was insufficient to neutralize a large amount of toxin, or (*b*) because the immunity conferred was of insufficient duration. In the first case tetanus appeared early; in the second case, late. Clinically the late forms of postseric tetanus were of interest and unlike the usual picture. Frequently spasms were limited to the locality of infection; in some patients, partially immune, the bulbo-medullary centers remained unaffected, but symptoms referable to cortical stimulation (hallucinations, delusions, etc.) occurred.

For the prevention of early postseric tetanus the author recommends that from 20 to 30 c.c. of antitoxin be injected every eight days for one month, together with wide excision of bruised tissue. The serum, he believes, is best given by the subcutaneous route. For the prevention of late postseric tetanus vaccination is recommended. It has been shown that foreign bodies may harbor living tetanus bacilli for over 200 days, symptoms therefrom appearing after late operation or on commencing massage, or following some mechanical disturbance to nearby tissues. Cases in which late treatment — operative or manipulatory—is necessary, should not only receive repeated antitoxin injections as outlined, but should also receive tetanus vaccine. The vaccine he employs is the toxin used at the Pasteur Institute for immunizing horses. He gives this toxin iodized, subcutaneously, in successive doses of 4, 8 and 12 c.c. (1 c.c. of a 1:10,000 solution kills a guinea-pig of 400 gm.); he has seen no serious reactions in man.

By means of antiserum given at eight-day intervals for a month he feels that protection is afforded for forty-five days. By the subsequent use of vaccination he believes a much longer period of immunity is conferred. By combining the two in appropriate cases he is of the opinion that adequate protection against both early and late tetanus is afforded.

AYER, Boston.

THE EXISTENCE OF THE TWO DISTINCT PHYSIOLOGICAL SYSTEMS FOR THE TRANSMISSION OF MOTOR IMPULSES IN PERIPHERAL NERVES. J. RAMSAY HUNT, M.D., Brain, **41**:302 (Nov.) 1918.

Hunt's studies have led him to formulate the hypothesis that the skeletal musculature is enervated by two distinct systems of motor fibers. One system is under the control of the corpus striatum and subserved by a strio-spino-neural system. Its function represents a primitive and diffuse form of motor activity characterized by automatic and associated movements. The system is termed paleo-kinetic. The other system or neo-kinetic system phylogenetically more recent is under cortical control and subserved by a cortico-spino-neural

system. The highly specialized motor function of this system transmits isolated synergic movements.

The previous studies of this writer on paralysis agitans indicate that the extrapyramidal motor system is under control of the corpus striatum and that loss of the large motor cells in this structure occasions a break in the striospinal system causing a progressive loss of certain automatic and associated movements. Paralysis agitans is the counterpart of the spastic paralysis following pyramidal tract lesions. The writer developing his theories continues this differentiation of motor pathways in peripheral nerves and differs with Sherrington in the conception of a final common pathway for motor impulses.

The writer draws an analogy between the two types of sensibility—epicritic and protopathic—comparing these to neo-kinetic and paleo-kinetic motor functions, respectively. In restoration of function following gunshot injuries it would appear that the first evidences of motility are of the character of associated movements. Hunt relates the following case: A man, aged 30, was injured by a cut from a circular saw involving the musculospiral nerve in the middle of the arm. No improvement following after the lapse of one year, an operation was done, the nature of which was unknown to the patient and which was followed by some improvement, but the usefulness of the hand was seriously impaired. At the time of Hunt's examination fifteen years after the accident, there was a typical wrist drop with a total paralysis for all isolated synergic movements in the distribution of the musculospiral nerve including the supinator longus. When, however, the hand was closed, as in making a fist, the musculature of the entire forearm and upper arm was contracted—supinator longus, extensors, and the hand assumed a position of extension. This phenomenon was interpreted as an expression of automatic and associated motor function and of either restoration or preservation of the motor system of fibers conveying this function; whereas the other system of fibers—the neo-kinetic system—had been permanently interrupted. The difference in the behavior of the different systems may be explained by the assumption that the paleo-kinetic system is not only less vulnerable but regenerates more readily after injury. A further similar musculospiral case is reported by Hunt, also a published case of Oppenheim; and references are made to three additional cases illustrating clinically this same phenomenon in the distribution of other nerves, for example, the median-popliteal.

In the restoration of motility after facial palsy the writer believes that there is additional clinical confirmation of his thesis. Dependent on the location of the lesion there are recognized two principal types of facial palsy: one characterized by spasticity and loss of isolated movement (pyramidal tract lesion); the other producing rigidity and loss of the automatic and associated movements (pallidal system lesion). The expression of emotion is essentially of the automatic and associated type, and the emotional enervation of the face is centered in the corpus striatum. Voluntary motion is dependent on the integrity of the cortico-spinal system.

From the anatomic standpoint attention is called to the theory of dual enervation of striated muscles as enunciated by Botazzi, also to the presence of another type of end-plate in striated muscles demonstrated by Boeke which is the termination of a nonmedullated fiber and is apparently of sympathetic origin. These sympathetic endings enervate the sarcoplasm of muscle which is that component concerned with the slow tonic forms of muscular contractions and is plastic in its function. The quick contraction or twitch is the function of the anisotrophic disk system supplied by medullated nerve fibers. The investiga-

tions of Langelaan and Sherrington show that these functions are entirely different from a physiology standpoint. It is believed by Hunt that certain differences in the function of the paleo-kinetic system and neo-kinetic system are closely related to this duality of function of the intrinsic muscle mechanism: notably, the twitch component is of more recent origin phylogenetically and has to do with isolated movements of cortical origin. Thus the anisotropic disk system could play a greater rôle than the sarcoplasm concerned with automatic and associated movements.

The studies of Ranson of nonmedullated nerve fibers in peripheral nerves, found in considerable numbers and thought by him to be concerned with the transmission of protopathic sensibility, are mentioned as suggesting and interesting similar study of motor fibers. Further, accepting the correctness of the theory which holds that in peripheral nerves there is a more highly differentiated form of nerve fiber subserving the neo-kinetic function one might expect a myelinization of fibers subsequent to birth as in the case of the pyramidal tracts. The studies of Hatai along these lines in the anterior roots of the white rat, and of Boughton on the oculomotor nerves of the same animal show that the number of medullated fibers increases as the animal becomes older.

Large-sized and medium-sized medullated nerve fibers predominate in the ventral roots of the spinal cord supplying the muscles of the extremities which are concerned with finer cortical movements (in proportion of 5 to 1). On the other hand, finer nerve fibers preponderate in the thoracic and coccygeal regions in the proportion of 3 to 1. These anatomic facts taken from Quain's Anatomy are cited in confirmation of the theory under consideration.

Returning to the clinical aspect of the subject, the two systems are related to the classic types of central hypertonus-spasticity and rigidity. The removal of inhibitory control over the spinal centers would result in these manifestations of hypertonus. Spasticity results from the removal of cortical inhibition and evidences the altered function of the neo-kinetic system through the anisotropic disk system. Spasticity is characterized clinically by the more elastic quality of the tonus, exaggerated tendon reflexes and clonus indicating a greater development of the contractile element of motility. Rigidity results from the removal of inhibition of the corpus striatum and evidences the altered function of the paleo-kinetic system through the sarcoplasm. It is characterized by a more uniform increase in tonus, is of a more waxy character, lacks the so-called clasp-knife tension of spasticity, and clonus and exaggeration reflexes are absent. Rigidity is typified in paralysis agitans, the isolated movements of cortical origin being merely masked. Attention is called to the deformity which is so characteristic in pyramidal tract lesions (Wernicke-Mann Type). The paralysis is one of neo-kinetic motility and for the reason that the extremities and chiefly their distal portions are affected, as this portion of the musculature represents the highest degree of specialization of cortical movements. Contrasted with this type, the deformity of paralysis agitans is concerned chiefly with the trunk and root segments and the paralysis of this disease is one of automatic and associated activities of muscles.

Consideration of the reflex activities in the two different central types of palsy brings out noteworthy differences when either the cortico-spinal or strio-spinal systems are involved. In paralysis agitans or an affection of the paleo-kinetic system the skin reflexes are unchanged as they depend on reflex activity of a higher type (afferents, epicritic sensory system, efferents neo-kinetic system). Also the tendon reflex show no special abnormalities, nor is clonus present. In spastic paralysis due to lesions of the cortico-spinal

system, the abdominal and cremasteric reflexes are abolished. The Babinski reflex which is of striate or strio-spinal origin replaces the normal plantar reflex. Striking is the presence of exaggerated tendon and periosteal reflexes and clonus.

Finally the cerebellum is considered as consisting of a paleo-cerebellum controlling the postural or static function of automatic and associated movements and a neo-cerebellum for the postural control of isolated synergic movements of cortical origin. These stand in relationship with the strio-spinal system and to the cortico-spinal system.

This important article of Hunt is worthy of analysis in that it is an attempt to correlate much that is recent and important growing out of numerous studies of the motor mechanisms of the nervous system. The author, by further developing his ideas concerning the function of the striate body, brings in review his wide and intimate knowledge of motor function to support his hypothesis. But, as the author himself admits at the beginning of his article, the theory is more suggestive than complete. It is founded more on clinical interpretation and theoretical considerations rather than on anatomic or physiologic facts or experimental evidence. The theory would appear to stand or fall on the existence of an anatomically distinct system of fibers in peripheral nerves centrally controlled by the striate body, with spinal and reflex connections and finally ending in a separate system of motor endings in skeletal muscles. Considered anatomically the evidence in support of his theory appears to be based on the demonstration of sympathetic nerve endings in striated muscles and the suggestion that the peripheral nerve connections might be demonstrated in some such manner as Ranson has demonstrated afferent nonmedullated fibers. It would thus appear that the strio-spino-neural system is in part at least sympathetic, yet this is not clearly brought out by the writer. Associated and automatic movements, function of the paleo-kinetic system would be a manifestation of sympathetic nerve function, under the control of the striate body. This would be the logical deduction if we follow correctly the line of argument. That the rigidity of paralysis agitans might be due to disturbed function (tonus) of the peripheral sympathetic system due to removal of central inhibition allowing fuller play of the plastic component due to sarcoplasmic activity is conceivable. There is some confirmation in this view perhaps by the rigidity observed by Sherrington in decerebrate animals, and believed by Langelaan to be due at least in part to a spasm of the sarcoplasmic part of the muscle substance. But that this same mechanism would also serve for automatic and associated movements appears to us to be too all-inclusive and especially as it is argued that loss of central control over the paleo-kinetic system would abolish these movements. In other words, removal of inhibition of the paleo-kinetic function would, on the one hand, cause hypertonus—a positive mechanism—and, on the other hand, abolish automatic and associated movements—also a positive mechanism.

Hunt believes that the twitch component concerned in muscular contraction and related to the anisotropic disk system has to do with isolated movements of cortical origin and belongs to the neo-kinetic system. Recent studies of tonus and reflex activity in uncomplicated cases of complete division of the spinal cord are not in accord with this view. For example, Riddoch observes in these cases an absence of the plastic component and a retention of the contractile element in the muscles. The patellar reflex is brusque and followed by a quicker relaxation phase as compared with cases of incomplete division that is, in the sense of Langelaan that the slow tonic component,

not the twitch component, is altered by severance from cortical control. It may be said, however, in this connection that in a case of complete cord section reported by Schaller the muscle tonus was normal or increased.

It is assumed that the paleo-kinetic system is less vulnerable to injury or regenerates more rapidly after injury thus explaining the first return of automatic and associated movements when function is restored. The cerebellum is divided into a paleo-cerebellum and neo-cerebellum for postural control of the automatic and associated movements, on the one hand, and isolated and synergic movements, on the other hand, without a clear exposition of the mechanism of these relationships. We thus discern a tendency to reason from this attractive hypothesis rather than to build an argument from accepted ideas of anatomy and physiology. Before we can accept Hunt's hypothesis we must have a more convincing demonstration of separate pathways for motor fibers in peripheral nerves.

SCHALLER, San Francisco.

WHY IS THE "UNCONSCIOUS" UNCONSCIOUS? MAURICE NICOLL, W. H. R. RIVERS AND ERNEST JONES, Brit. J. Psychol. **9**:230-247 (Oct.) 1918.

Rivers, after a delimitation of "unconsciousness," emphasizes this by a common instance of an experience, unconscious for thirty years, yet related to a persistent and marked symptom, reappearing in consciousness at the end of this period. "This active existence, apart from experience readily accessible to consciousness, is known as dissociation." His question are, "why experience becomes unconscious and why, having become unconscious, it should persist in this dissociated state. . . ." Rivers locates the solution in the life of the organism. He describes in the butterfly the formation in its larval stage "of a highly complex body of experience, based on a certain mode of progression and certain methods of obtaining and utilizing food." "So far as experience is conscious we suppose it takes part in the regulation and success of the life of the animal." He now sees, in the persistence in the consciousness of this experience into the next stage of existence, the liability of that which would impair those movements adapted to a now totally different mode of existence. "The perfectly adjusted flight of the butterfly could only be disturbed if memories derived from the larval state of existence entered into the consciousness."

He makes these examples of what less strikingly takes place in every animal, including man. A similar interference is seen in the more evolved organism through any persistence of earlier unmodified modes of consciousness. "The diversity of the different phases of the life history and the incompatibility of the reactions of one phase with another" is the reason why the conscious states become unconscious. He further sees this suppression or dissociation as peculiarly complete in those organisms where there is absolute dependence of the animal on instincts. Its high point in man occurs also with those years where the conduct depends largely on inherited impulses directly related to the primary needs of life. "It becomes a question whether the dissociation of the mental life of Man is not a mode of reaction belonging originally to its instinctive aspect which has continued to be utilized after this aspect has been largely replaced by intelligence or reason. Dissociation would thus be a state especially prone to come into existence whenever it is required to put instinctive modes of reaction into abeyance, to suppress instinctive modes of behavior which would interfere with the harmony of an existence based on less immediate and more modifiable reactions."

Yet the biologic mode of dissociation he notes as having been modified, for, obviously, affective responses, as of the infant, appear ready to present if later conditions call them forth. In place of the complete suppression there comes into existence a mechanism whereby certain parts which were useful could be utilized, while others were dissociated. He sees this principle permeating the whole of evolution. The process of repression of the psychologist corresponds exactly to the inhibition of the physiologist. "Nature has always utilized existing structures and functions, combining the new with the old, utilizing what she needs and inhibiting those parts of the products which would interfere with the normal action of the new. The symptomatology of disorders of the nervous system mainly depends on the coming to the surface under pathologic conditions of those older and cruder activities which have been controlled or suppressed by the later products of evolution."

Thus seen, repression (for here is the core of largest use in this discussion) is something close to an instinct; its function is to put out of the running other instinctive modes of behavior which interfere with the mechanism made up of a combination of instinctive with intelligent modes of reaction. This makes, as Rivers says, the unconscious the home of the instincts. With this endeavor to discover some "biological archetype" for the processes of suppression and repression, Jones immediately expresses an approval. He perhaps is right in holding Rivers' examples as over-remote. But his shrewdest and broadest critique lies in his statement that, "in the endeavor to establish a purely utilitarian basis for the exclusion of unconscious mental processes, Dr. Rivers has been too much influenced by the English biologic doctrines of the nineteenth century, which, as is now known, interpreted all vital processes too exclusively in terms of survival value." Aside from the difficulty in bringing the phenomena under this head of utility values, he properly defines our necessity for stating them in a preliminary way in terms of affects. What Rivers called the incompatibility between instinct and intelligence, Jones relates as of a hedonic nature. Yet there is a definite aim here on Jones' part in considering the possibility of an approximation of views in the examination of the ultimate sources of repression. In approaching this he develops in a clear form the notion of Freud's primary and secondary systems, a notion here described as avowedly tentative.

Looking at the wish—a "gigantic reflex"—as, in the mental sphere, the expression characteristic of all activity to restore a disturbed equilibrium, he pursues its route in the primary system with the later initiated activity of the secondary system coming on the heels of the "bitter experience of the inadequacy of the first hallucinatory gratification." The second inhibits the movement of physical energy; the primary allows the freest possible movement throughout the entire system; whatever is disagreeable is ignored, for only the fulfilment of the wishes is permitted. This latter course is not possible for the secondary system. In this theory of Freud's, with which the reader is familiar, Jones sees, in the interrelation of the two systems, that which falls in well with Rivers' utilitarian principle, for the gain to the organism is evident in the subjection to the reality principle belonging to the secondary system of the hedonic principle appertaining to the primary. There is here a guidance and inhibition of one kind of activity by another which in evolution has come to be superimposed. Probably, also, Jones defines the reality principle in its evoluting position as functioning to extend and elaborate the pleasure principle. This he emphasizes as something over and beyond its functioning as a utilitarian value.

A difference in concept appears at this point. The examination of ultimate sources has given a considerable agreement between the biologic notion of Rivers and the expressions of the Freudian theory of the mental systems. Perhaps the difference is a bit fictitious and necessitated by the guiding lines of conscious and unconscious, necessitated by the discussion. The two systems are viewed as the precursors of the unconscious and conscious mind of later life. The point here is not strong as, in Jones' statement, "the mind of the infant can hardly be called either unconscious or conscious, though probably it is nearer to the former." Certainly the notions of the primary and secondary are to be read in the relation of conscious and unconscious, to the benefit of the latter term, as in his defining of the inadequacy of the secondary system at all times to inhibit and control due to its rapid growth and changes, resulting in a sharper contrast between the instinctive or infantile and the higher standards of the later secondary system. Yet in the point of the secondary system serving the primary, though controlling it, appears the presence of the wish and the hedonic quality present. That he places this at a later point than the "utilitarian" function, is to be noted and approved. The arresting fact lies in the extension of the concept of repression beyond that usually connoted. A biologic connection is here suggested of considerable heuristic value.

Both Rivers and Jones are rather severe in their consideration of Jung's theories as presented by Captain Nicoll. The notion of the unconscious as an inheritance, a racial background of the mind, as a collective unconscious with the personal unconscious, "an excerpt of the collective containing repressed material that has an intimate personal significance," this naturally would fall across the line of both his fellows in the discussion. "The unconscious is unconscious because it is not yet fully adapted to reality." Jones remarks on this view as to its being not yet adapted, that, from Captain Nicoll's lofty conception of the nature of the unconscious, one might expect that it easily would be. Also he refutes, in his critique, the notion imputed to Freud that all unconscious processes have at one time been in the individual's consciousness. "The sources of conflict lie in the unconscious; here are forces of progression as well as forces of regression": these statements of Nicoll give the whole notion of evolution a location, a special site, in consciousness. While Rivers sees in the unconscious a storehouse of instinctive activity, more or less incompatible with later products of evolution, Nicoll, after Jung, sees "an inexhaustible reservoir with which man is provided at birth and from which he can draw material for his psychic development." Yet this peculiar diversion of concept throws into clearer relief the essential qualities of the discussion, earlier presented, wherein both the ideas of the unconscious have been defined through the notions of the dynamic mechanisms of repression, while the latter itself has gained considerably in depth of background.

PARKER, New York.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Three Hundred and Seventy-First Regular Meeting, held at the Academy of Medicine, March 4, 1919

WALTER TIMME, M.D., *President*

BILATERAL FRONTAL HEMORRHAGE WITH MENTAL AND PHYSICAL SIGNS PRECEDING AND ACCOMPANYING THE HEMORRHAGE. Presented by DR. FREDERICK J. FARNELL, Providence, R. I.

This case was that of a woman, aged 49, whose make-up, as far as could be ascertained, had always been considered normal. With a clear history of no previous attacks or upsets she developed a mental state not unlike the manic form of manic-depressive insanity, which settled, after several months, into a hypomanic condition. Physically there was hypertension; blood pressure 210 systolic and albumin in the urine. Approximately twelve months after the onset of the so-called functional psychosis, she had a cerebral hemorrhage with clinical signs suggesting the intraventricular type. This was followed by a complete change in the mental picture. From a functional psychosis with thought (thinking) disorder, she settled into an organic psychosis with an obstructive disorder, or an intellectual loss. The physical state then improved and she was soon up and about, but there was no change whatever mentally. In five or six weeks signs of cerebral compression developed and ultimately contributed toward her death.

The interesting features might be grouped as (*a*) mental and (*b*) physical, in an individual who developed two psychoses. Her first aberration was characterized by emotional elevation, acuity of emotional response and quick recognition of logical judgment and even, at times, critical judgment. Following hemorrhage this emotional state changed entirely into an actual loss with those accompanying behavioristic traits which so characterize the personality of organic brain disease; deterioration in feeling, instinct, conduct, etc. Then, too, such organic functions as intelligence, judgment, insight, etc., which in her primary psychosis were only interfered with to the extent of thought disorder, too many thoughts coming at once were practically completely destroyed in her second psychosis.

The initial physical disorder was limited to hypertension and albumin in the urine. The second physical disorder was considered as a symptom-complex related to the ventricles. The third physical complex was a syndrome indicating cerebral compression. Pathologically the brain (which was exhibited) showed bilateral mid-frontal hemorrhage with organization, secondary necrosis and softening of the brain tissue itself.

These facts were offered for consideration, especially so to those whose interest lay in the field of psychopathology with special reference to personality and psychosis, and in addition, to the histo-pathologist to whom interest would be manifest in the fact that the lesion was bilateral and the vascular sclerosis localized in the cerebral vessel system.

DISCUSSION

Dr. Smith Ely Jelliffe asked if Dr. Farnell might have something to say about the hypertension states with increased blood pressure and the relationship of their emotional causes to cerebral hemorrhage. In one of the discussions on psychanalysis held before the Neurological Society recently, the speaker presented the situation of a case of autonomic responses to unconscious emotional stimuli, and spoke of the tendency of these cases to develop these cerebral hemorrhages. He said that the psychotherapeutic mode of approach could be very successfully pushed with the hope of reducing the hypertensive state by getting at the emotional causes for it. He had taken occasion at that time to discuss rather briefly what some of the problems were and related the partial history of a patient who had a blood pressure of 235 systolic, with almost *petit mal* lapses, who was correctly diagnosed by an internist as a nephritic and given six months to live. What it was that lay behind the clinical picture was not discovered nor even sought for by the internist who made this diagnosis, the dynamic reasons for the hypertension nephritis. When the dreams were investigated the cause for the distress of the patient was quite apparent; the unconscious was engaged in a sadistic attempt to destroy everything about her and the result was that she was destroying herself. If it had kept up, she might have died, if not of nephritis, of a cerebral hemorrhage as had Dr. Farnell's patient. The psychanalytic mode of approach offered a dynamic pathology which was not in the usual ken of the internist and proved its value in these nephritides with their disturbed emotional undercurrent as the real dynamics of the situation.

Dr. I. Abrahamson said he would like to know more about the behavior of the reflexes. That all reflexes were absent after the bilateral hemorrhage in both ventricles he knew, but it was not clear to him whether they returned after the condition cleared up and, if so, the order of their return.

Dr. Clarence O. Cheney questioned whether the hemorrhage was of the intraventricular type, for the specimen did not seem to show evidence of a breaking of the ventricular wall; it looked rather as if the ventricles had been compressed by the hemorrhage. The absence of blood in the ventricles would have accounted for the absence of blood in the spinal fluid. He recalled one case necropsied several years ago which showed intraventricular hemorrhage causing sudden death and believed that if a hemorrhage of the size demonstrated in Dr. Farnell's specimen had entered the ventricles immediate death would have resulted. The distribution of the hemorrhage suggested that it had originated from one of the anterior cerebral arteries.

Dr. Farnell, in answering the discussion, replied to Dr. Jelliffe's question regarding the hypertension that, although the patient had a blood pressure of 210 systolic with albumin in the urine on admisson to the hospital, the albumin soon disappeared. The hypertension continued until after the hemorrhage, and from that time until death the blood pressure was below 160 most of the time. With reference to the emotional factor and its responsibility for hypertension and nephritis, it was impossible to do an analysis of the patient, for even when she settled into the hypomanic condition she was beyond reach of questions and psychic control. Answering Dr. Abrahamson's question as to the reflexes, they returned and became exaggerated, that is, all deep reflexes became exaggerated. The superficial reflexes returned and even when she was up and about she had exaggeration of reflexes, double ankle clonus and double dorsal extension of the great toes. Ten days before death she was

again minus all reflexes. She was in a deep stupor with signs of cerebral pressure. Muscular flaccidity with abolition of reflexes was again marked, and the condition then and at the time of the hemorrhage was noted by all the men who examined her. The physiology could not be explained beyond its being a question of first hemorrhage and pressure, and second organization and pressure. The clinical diagnosis made at the time she had the hemorrhage was bilateral ventricular hemorrhage, at least, the symptom-complex suggested that, though there was no blood in the cerebrospinal fluid. That might seem impossible, but for two years the speaker had been examinng the spinal fluid of cases of cerebrospinal meningitis, and it was not uncommon for this syndrome to give intraventricular symptoms from accumulation in the ventricles of fluid or obstruction to the flow.

THE TONUS OF AUTONOMIC SEGMENTS AS THE CAUSE OF ABNORMAL BEHAVIOR. Presented by Dr. Edward J. Kempf of St. Elizabeth's Hospital, Washington, D. C.

Dr. Kempf (by invitation) delivered this address in which he traced the causes of abnormal behavior to physiologic facts. The evolution of man from the lower biologic types was sufficient reason for giving the primitive autonomic apparatus the greatest emphasis in formulating a conception of the personality. The lowest biologic organisms have a relatively highly developed autonomic apparatus, but a poorly projicient apparatus as the instrument by which the autonomic apparatus masters its environment. The old assumption that "the brain is the organ of the mind" is entirely unsatisfactory for localizing or explaining the dynamic forces that make up the personality.

The autonomic apparatus, as herein conceived, is constituted of the digestive, circulatory, respiratory and urinary system, the glands of internal and external secretion and their ganglionic nervous systems; that is, the ganglionic nervous systems lying outside of the brain and spinal cord and those ganglionic types of centers embedded in the brain stem and spinal cord. It is obvious that this is the apparatus that regulates the accumulation and assimilation of energic products from the environment, regulates their transformation, distribution and use, and the elimination of the waste products. It might be said that these processes constitute about all the fundamental functions of living, and that the striped muscle apparatus and its cerebrospinal nervous system had been developed in order to obtain the necessary means from the environment.

The physiologic researches of Cannon and Carlson on the peripheral origin, in the stomach, of the craving for food, as a typical acquisitive-assimilative compulsion, and Mosso's and Pellacani's experiments on the postural tonus of the bladder, show that when the grip of the bladder wall on the inert contents raises the pressure to over 18 c.c. a type of localized itching is aroused which constitutes the desire or craving to urinate, and which, as it becomes vigorous, compels the organism to behave so as to relieve the hypertension of this segment. This may be considered to be a very typical emissive-avertive type of compulsion. All compulsions to act are either acquisitive or avertive in relation to the environment.

Freud's suggestion, that all emotions and sentiments are really cravings, is further borne out by the studies of Cannon and others on the physiologic changes that occur when the individual feels "fear" or is said to be "afraid." Since certain types of gastric contractions cause the intragastric itching felt

as hunger, it is consistent to consider that other changes in the gastric functions, such as diminution of peristaltic functions and the maintenance of spastic tensions, when the individual is exposed to some type of actually injurious or potentially injurious stimulus, arouse an afferent stream that is more or less painful and disagreeable—that is to say, fearful. It is obvious that only those primeval animals or rather autonomic systems that felt distressing, fearful tensions, sought to protect themselves and so, by surviving in the struggle for life, have transmitted this fundamental attribute or function to man.

Wertheimer's experiments on the unconscious anesthetized dog, in which he injured the sciatic nerve in a manner that would surely cause pain in a conscious animal, shows that gastric changes occur which are very similar to the fear producing tensions, without the faculty of perception, to arouse the emotion, being present. This shows that at least certain cerebral integrative activities which enable peripheral activities to coalesce into perceptual images (or thoughts) are not necessary to cause many of those definite, important, autonomic tensions which, if the animal were conscious, would certainly cause it to be aware of very disagreeable (fearful) visceral feelings.

Like *fear* the other primary affective cravings, such as *anger, love, shame, disgust* and *sorrow* have their origin in characteristic peripheral disturbances in various visceral segments, and these peripheral disturbances are constituted of changes in the muscular activities, particularly the tensions of the viscera, stimulating the local sense organs. This means that it is of the utmost importance to recognize that our affections are symptoms of autonomic tensions and activities and we must practice visualizing these activities behind the symptoms that we see or hear complained of.

These autonomic-affective tensions set up afferent streams of nerve impulses which, as the autonomic component (Langelaan), contribute greatly to regulating and sustaining the postural tension of the striped muscle apparatus, and the tension of the striped muscles in turn stimulate the proprioceptors embedded in the muscles and tendons and about the joints, setting up converging kinesthetic streams which coalesce into images and concepts, that is, the mental pictures constituting most of the content of consciousness. In a sense we think with our muscles.

The present controversy between Langelaan, de Boer, von Rinjberk and J. G. Duesser de Barenne as to the exact manner and through what channels this influence is exerted is not so important for psychology and psychiatry as the fact that it does occur in some *quick, intimate* manner and follows the law of the autonomic-affective apparatus striving to maintain a state of comfortable tension with the greatest economy of extent and duration of effort. This law may be formulated as follows:

As the autonomic-affective apparatus is forced into a state of unrest, either through metabolism or endogenous or exogenous stimuli, it compels the projicient apparatus to adjust the receptors in the environment so as to acquire stimuli that have the capacity to produce comfortable postural readjustments in the autonomic apparatus. For example, when the autonomic apparatus of a child assumes fearful tensions because of the barking of a dog the affect from these tensions compels the child to run to its mother who, as a soothing stimulus, readjusts the tensions. So too, the business man takes out insurance as the soothing stimulus, the fearful sinner goes to church, the savage and the modern speculator wear charms and fetiches, in order to counteract the fearful stimulus existing in his expectation of a disastrous fire, storm or coincidence.

Von Bechterew has shown that various autonomic segments and even the simple striped muscle reflexes become conditioned by experience to react to certain stimuli. This occurs by the reflex being aroused by the primary stimulus while it is associated concomitantly with other stimuli which ordinarily have no effect, but which, after repeated simultaneous association with the primary stimulus, come to have the same influence on the reflex that the primary stimulus had. For example, when a child going barefooted for the first time in the grass, steps on a bee which stings its foot, the child, for some time after this experience, has strong autonomic fear reactions which prevent it from walking on the grass while barefoot. Here then the grass, formerly a pleasant stimulus to the bare feet, by being associated with the bee sting comes to have the capacity to arouse strong autonomic fear reactions. It becomes a painful stimulus, while to other children it is a pleasant stimulus. We can readily see how, by experience, the individual segments of the autonomic apparatus of an individual becomes conditioned to react to stimuli that have little or no effect on other people and determines most of our eccentric or individualistic preferences and prejudices, our "taste," hobbies, phobias, obsessions, compulsions, vocational pursuits, etc. No doubt all our selections and aversions for simple things and for complicated things, that are immediately present or that may arise in the future, are greatly determined by your autonomic-affective cravings having been conditioned by previous painful or pleasant experiences to seek or avoid the future possibility.

Since all the autonomic segments must obtain their stimuli through the proper exposure of the favorite receptors, for which they have become conditioned, there is an incessant convergence on and striving for control of the final common motor paths, and our complicated stream of thought and overt behavior must be seen as the resultant of these converging forces. When any particular autonomic segment becomes hyperactive and tends to dominate the autonomic union and obtain control of the striped muscle apparatus the individual becomes conscious of a definite stream of thought which is symptomatic of the activity (as gastric itching—hunger—thoughts and acts about when, where and how to get food; cystic itching—craving to urinate; reversed gastric and esophageal peristalsis and feelings of nausea with avertive compulsions for a particular odor, vision, taste, person, or suggestion).

It follows logically that if one autonomic segment becomes thoroughly conditioned to react in a distressing manner to certain stimuli, and other autonomic segments become thoroughly conditioned to react in a pleasant manner to certain stimuli, whenever the individual happens to meet those two groups of stimuli associated together in a situation, he will feel a confusion of tensions with compulsions to seek the advantages of the situation as well as compulsions to avoid it. For example, a young married man complained that although he was fond of his wife and desired to be loyal and faithful to her, that "such asinine things" as the hair on her legs caused him to lose his sexual excitement (depression of the tonus of an autonomic segment) which irritated him exceedingly. Many of the attributes of his wife, such as her wit, sense of humor, facial expression and coyness, as stimuli had a decidedly invigorating effect, but when he made further approaches he met with a stimulus that had quite the opposite effect. He finally compelled his wife to shave her legs in order to remove the distressing stimulus. We see here how the autonomic apparatus—looking at it in a biologic sense—compels the love object to remove or avoid stimuli that jeopardizes its potency as well as seek stimuli that tone up the autonomic segment.

At birth we have a perfectly organized but unconditioned autonomic apparatus with a very poorly coordinated projicient apparatus. The autonomic apparatus begins immediately to organize the projicient apparatus to suit its cravings in their struggle with the environment, and we see this process continuing throughout life as the individual develops his education, vocation or profession. For a considerable period after birth the infant indulges *heedlessly* in its segmental pleasures, such as nursing, urinating, defecating, cooing and screaming, without regard to the interests of other people. But these indulgences soon become an imposition on many of the autonomic interests of its parents and its social group, and they in turn are compelled to exert an incessant pressure on the infant which eventually conditions and more or less conventionalizes its methods for acquiring gratification for its segmental pleasures. Thus the infant gradually becomes conditioned to avoid the loss of favor and esteem of its parents and playmates because, when in disfavor, it is subject to many distresses, such as physical punishment, humiliation, lack of petting, feeding, etc. On the other hand, by behaving in a manner that wins favor and esteem from its associates, many of its segmental cravings are more easily gratified, such as cravings to be petted, played with, fed, given preferences. Gradually we see the infant changing from heedlessly enjoying its segmental pleasures to secretly doing so, such as nocturnal bed wetting. Then as the *ego* develops, the coordinations to control them entirely, in order to prevent the loss of esteem, become apparent. That is, the segments of the autonomic apparatus which are similarly conditioned gradually become integrated into a unity to prevent any hyperactive segments from jeopardizing them. This process of integrating into a unity is a *compensatory* reaction to prevent getting into the *fear, shame, sorrow* or *anger* state; autonomic compensation being one of the most fundamental attributes of living tissue.

The development of the *ego* begins as soon as the infant begins to fear to lose the favor and esteem of its comforters and protectors by becoming inferior (organically or functionally) to a competitor, or by self-indulgently yielding to oral, anal, urethral, etc., pleasures, by sucking, defecating, urinating, screaming, stealing, lying, etc., without regard for the feelings of others.

Any form of fear or pain no matter how mild or indirect the cause, initiates more or less of an autonomic compensatory reaction; hence, the individual's incessant compensatory striving to learn to help and improve itself is really *the autonomic apparatus striving to avoid getting into the malnutritional fear, shame, or sorrow state.* In due time this incessant striving, to avoid the stream of incessant interrelated fear-causes that confront the child during the day, becomes knitted or integrated into a complicated unity that eventually comes to regard itself as "I," or the *ego* and its various segments (teeth, eyes, stomach, etc.) as "mine." Now the perversely conditioned segments that jeopardize the *ego* become outlawed as "not mine," or sinful, evil, the devil, "hypnotic influences," "secret forces," etc.

Serious and fatal interautonomic conflicts occur when most of the apparatus is conditioned to strive for biologically and socially estimable things and one or more vigorous segments becomes intolerably or *perversely* conditioned. This is the foundation of the anxiety neuroses, the benign and pernicious psychoses and many forms of criminal or asocial adjustments. This constitutes the conflict between the *ego* and the *not-ego,* that is, the struggle between the autonomic apparatus, coordinated into an egoistic unity or personality, striving to win social esteem, and the self-indulgent segmental crav-

ings that only crave for the counter stimulation that neutralizes or gratifies their tensions; as in masturbation, sex perversions, envy, gluttony, slothfulness, etc.

The *ego* can only control the jeopardizing segment by preventing it, more or less, from using the final-common-motor-path or striped muscle apparatus to acquire what it needs. When the jeopardizing craving is permitted to cause the *ego* to be conscious of its needs but is not allowed to act, it is *suppressed*, and when it is also prevented from causing consciousness of its needs, it is *repressed*. The suppressed and repressed hypertense segments, like compressed springs, exert an incessant, severe pressure to break through the resistance and obtain gratifying stimuli. This is shown in sudden changes of purpose, selections, obsessive thoughts, errors, accidents, misinterpretations, dreams, delusions, hallucinations, mannerisms, old memories, deliria, etc. By a *summation* of the repressed cravings, or the fatigue or weakening of the repressing *ego*, a dissociation of the autonomic apparatus or personality occurs and the ego is forced to struggle with all sorts of compulsions, delusions, hallucinations, etc.

Here then lies the psychopathic struggle. The fear of the loss of social esteem initiates the compensatory striving, which, because of the vigor of the fear of the influence of the repressed, tense, autonomic segment, becomes progressively eccentric, finally causing the loss of the confidence and esteem of the social group. Now a vicious affective circle is established which tends to eventually destroy the socializing capacities of the personaltiy. Gradually as the *ego* becomes more and more asocial the erotic segment obtains complete control of the personality .

A photograph of the perpetual motion machine of a paranoid negro was shown to illustrate how fear of the loss of sexual potency and of becoming an oral erotic homosexual initiated the eccentric, compensatory, divine inspiration (a truly biologic compensation) to build a "perpetual motion machine" which would make him a great prophet, allow him to found a faith, have many wives, etc. This perpetual motion machine is called the "first church" . . . "where the blood of the world is mixed," and is a simple copulation fetish.

Photographs of so-called hebephrenic dementia praecox cases showed the women squatting like apes and the incessant attention and frequency with which their hands counterirritated the urethral, anal and vaginal zones showed how, as biologic types, the anal and genital autonomic segments had destroyed the ego and dominated the autonomic apparatus.

Another photograph was shown of a soldier who carried his foot over his anus. He had passed through an anal erotic homosexual panic in which his delusions and hallucinations of being assaulted were caused by the anal erotic cravings (like gastric cravings and thoughts of food) seeking appropriate stimuli and his defense against the compulsion was a violent functional distortion compelled by the autonomic apparatus, as a compensation, in order to protect itself from going into the fearful state. He anxiously protested that he would go "mad" if the leg was straightened out.

DISCUSSION

DR. SMITH ELY JELLIFFE said that the point of view presented by Dr. Kempf struck a responsive chord in his own thoughts, and he had certainly performed a signal service in that he had bridged successfully two parallel lines of interpretation which were found throughout the medical community.

There were those who held that mental causes and somatic causes ought to be considered as separate types of activity. Not only through this presentation, but through Dr. Kempf's work on "The Autonomic Factors in Personality," these two parallel trends had been made to merge and a synthesis was presented whereby one could understand the individual working as a unit. What Dr. Jelliffe had to say he would confine to a few points, one of which interested him a great deal because it so frequently came up as a point of issue between these apparently parallel types—the question of infections, autointoxications and focal infections. Perhaps some of those present would recall an illustration of this, a patient who having suffered from a severe compulsion of washing the hands came for treatment at the age of 52, the compulsion having existed since she was 18 or 19 years of age. In the early days of the compulsion the washing of the hands was associated with certain prayers for purity, cleanliness and holiness, and she got along very well, the personality adjusting itself. At the age of 23, however, she had an attack of influenza and immediately the depressing effect of the influenza toxin broke down the adjustment of the hand washing and the prayers and she developed two new symptoms—diarrhea and auditory hallucinations in which obscene voices made vulgar references to defecation. If one conceived of an individual having 65 per cent. efficiency and a loss of 35 per cent. in a range of 100, the handwashing and prayers took up the 35 per cent. of the loss under ordinary circumstances, but when the influenza toxin came along, 10 per cent. more load was drawn on the autonomic segment adjustment, the diarrhea representing 5 per cent. and the hallucinatory projection representing 5 per cent. As a result of the strain she made a suicidal attempt. Ten years later another attack of influenza produced a similar result with diarrhea and hallucinatory voices which took on a more erotic form. Later, at the age of 52, a partial analysis enabled the patient to partially understand the compulsions as anal-erotic components in the personality. In an attack of influenza following the analysis she developed a diarrhea, but did not hear the voices and made no more attempts at suicide. At 52, she was much better able to handle her autonomic segment maladjustment thrown out of gear by reason of the toxin of influenza.

It was not influenza toxins, nor poisons from the intestines, nor infected tonsils that produced these situations in so many, but they should be considered as partly accessory in the breaking down of the combination. The real difficulty was the personality difficulty and the infection or toxemia was an additional factor to that difficulty. Furthermore, Dr. Jelliffe said that he thought that the original personality difficulty, if it could be analyzed out into its original roots, would afford a clue as to reasons why the infection or the toxemia could localize its effects in certain autonomic segments. Such autonomic segment neural pathways were under constant tonal maladjustment; they were overactive in the attempt to effect healthy functioning in the segment in spite of the instinct distortions, due to the conditioned segment stimulus to early emotional stimuli. After many years of such faulty strain in the reciprocal activity of the two components in the vegetative arc, the resistance of the tissues under the neural innervation in this arc were so seriously undermined as to permit of localization of an infecting or toxic agent in that arc. This was a local anaphylactic sensitization. Thus the localization of the disease in the badly functioned autonomic segment.

Dr. Jelliffe spoke of the influence of faulty anal neurotic stimuli, under constant repression, and the possible determination of rectal crises in tabes, localizing themselves as rectal rather than other types of crises because of

this autonomic struggle. An illustration was cited in which a partial uncovering of a passive pederastic unconscious repression in a tabetic with rectal crises possibly precipitated an intense delirium with fecal content. The speaker said he was simply following the clue which Potzl, Adler and others had offered in their attempt to answer important questions concerning why one or another organ or special parts of an organ were involved in a diseased process.

Dr. Adolph Stern considered Dr. Kempf's presentation especially interesting from the point of view that, as suggested by Dr. Jelliffe, it served to bridge over two apparently conflicting conceptions of mental (emotional) processes, namely, the physical and psychologic, by giving the physiology of the emotions. This conception of Dr. Kempf, explained in concrete form, gave the physical basis for various (neurotic and psychotic) symptoms, which were in a measure, understood by psycho-analysts and explained by them as physical manifestations of thought processes. These now had a physiologic explanation as well.

It was also very instructive to find that the laboratory experiments on animals by Cannon, Crile, Sherrington, and others served to establish on a firm foundation the concept of the unconscious or autonomic system as presented by Dr. Kempf. Cannon especially has demonstrated the bodily changes that accompany the strong emotions and the instinctive cravings. Judging from the sensations as described by patients suffering from neurotic symptoms in the form of bodily sensations, that is, various paresthesias, etc., it was now known that such sensations were not at all "imaginary," but that they had a definite physical, physiologic basis consisting in a change, in the region in which the sensations were felt, from the normal tonus maintained by the autonomic system, the change being one determined by the emotions present at the moment.

Referring to the "condition reflex" and its bearing on psycho-analysis, a certain patient bore for many years a more or less conscious hatred for his father. He was always very irritable and easily incensed at any attempt to give him an order, even though he complied readily enough. He was very ambitious, the ambition being in a great measure a desire to be superior to his associates. Failure in any ambition was always accompanied by anger at the successful individual, whose ability he depreciated. This patient was aware of a general sense of tension of all muscles of the body, especially the arms and face. He frequently, without any conscious cause, doubled his fist and smote the palm of his other hand. On analysis he disclosed that the peculiarities noted were determined (conditioned) by the unconscious attitude he bore toward his father to whom he attributed motives present in his own mind. Qualities present in people recalling to the patient those he saw in his own father determined the attitude of the patient toward these people. This state of affairs extended over many years and the emotional state was of similar duration. Applying to this what Dr. Kempf taught, this patient's autonomic system would seem to be "conditioned" by attributes he saw in people suggesting unconsciously those possessed by his father, causing a change in the normal muscle tonus sufficient to bring about muscular discharge, that is, striking of palm with fist. This change of tension was the "feeling," in the present instance, of anger felt by the patient as a disagreeable sensation, the origin of which was unconscious to him. This gave a physiologic explanation for that which Freud empirically designated as an "unconscious wish." To him it was a psychologic phenomenon, and it was

gratifying to substantiate his clinical findings by means of physiologic data. In the case just cited, the more or less unconscious hatred for his father, his pathologically motivated ambition, his rebellion to authority, all were accompanied by an unconscious wish to remove a rival, that is, the irritating stimulus. This was the unconscious wish.

Dr. Foster Kennedy thought that it might be of interest to some of the members of the Neurological Society in this connection to hear of two soldiers who were under his care last year and who exhibited in a very astonishing manner a cooperation of endocrinologic disturbance and emotional disturbance. These men were admitted to the hospital with complete emotional collapse after having been blown up without physical injury. They were in identical conditions, almost mute, almost inaccessible; it was difficult to make them eat and emotionally they were given over entirely to the phenomenon of fear. In both cases the hair was standing erect on their heads and remained so for nine days. The hair of both these men was long and stood on end like that of a Zulu. After a few days rest in bed they recovered their usual mental and emotional balance and were able to state in each instance that their hair previously was normally tractable and flat.

Dr. Bernard Glueck thought that every one should become familiar with Dr. Kempf's monograph on the "Autonomic System in Its Relation to Personality" because of the very helpful synthesis he had accomplished of the various physiologic and psychologic researches into human conduct. He had occasion recently in teaching psychopathology to his students at the School for Social Service to use this monograph very effectively, and found it very helpful in approaching this subject from the physiologic standpoint as outlined therein. It made very much more acceptable to the average mind the central theme in the freudian theory of conduct—namely, the wish. Dr. Kempf's discussion of the place for the craving of social esteem in human conduct was particularly illuminating, as it frequently was found to be the most prominent factor in problems of social maladjustments.

Dr. S. Rothenberg thought that every one present was indebted to Dr. Kempf for his splendid presentation and he personally appreciated it, particularly because of having done some work in attempting to interpret the so-called mismating complex from a psychosexual point of view. This work was done at the National Desertion Bureau in New York. He found there were decided and peculiar condition reflexes in many of these people who could not adjust themselves to the marriage state, which would explain the underlying difficulties better than in any other way. Many interesting instances of that kind had been noted.

Dr. Kempf, in closing the discussion, expressed his gratitude for the kind appreciation given him. He thought that the hallucinations in Dr. Jelliffe's case could be interpreted as an auditory hallucination caused by the anal segment, which had become dissociated, trying to obtain the necessary stimulus for gratification. He had been forced to the conclusion that one could not get a psychosis from an organic or toxic cause in which the primary autonomic affective cravings had not been previously repressed. The study of paretics, deliria and arteriosclerotics showed that strong autonomic compulsions, which had been repressed or were perversely conditioned, had become dissociated and caused the hallucinations, etc.

Dr. Jelliffe's point about the localization of disease processes in repressed segments might be explained by the fact that an autonomic segment which

was more or less anemic or hyperemic, due to the vasoconstriction or vasodilation in this segment which existed because of its repression, disease, or over-tension, became a more fertile soil for bacteria.

As far as therapeutic principles were concerned, there were two schools; one believed in building up the health, confidence, self-control and integrity of the ego, and the other in getting a *transfer* from the ego so that it would no longer be afraid of allowing the repressed craving to cause awareness of its efforts. With the transfer, the patient became conscious of what his personality craved and by learning to analyze and know himself, he became able to make much more comfortable practical adjustments, without becoming fascinated by bizarre, asocial, or perverse stimuli.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, March 20, 1919

HUGH T. PATRICK, M.D., *President*

EXPERIENCES WITH THE AMERICAN RED CROSS IN ITALY.

DR. RALPH C. HAMILL addressed the Society on this subject.

TWO OPERATED CASES OF EXTRADURAL TUMOR COMPRESSING THORACIC PORTION OF CORD.

Presented by DRS. CARL B. DAVIS and PETER BASSOE.

CASE 1.—*Summary.—Paraplegia of two years' standing; loss of all sensation below the level of the fifth thoracic segment; visible and palpable subcutaneous tumor corresponding level of back. Operation: Removal of hour-glass shaped lymphosarcoma, partly intraspinal, connected with external tumor through two intervertebral foramina.*

History.—A woman, aged 49, was seen by Dr. Bassoe on Jan. 24, 1919. In January, 1916, she began to complain of pain in the scapular region radiating around to the chest. The pain gradually grew worse. Unsteadiness of gait was noticed in June, 1916. Later the legs grew weak and after February, 1917, she could walk only with crutches, and early in 1918 became bedridden. Numbness in the toes began in January, 1918, and ascended. Control of the sphincters was lost at the time she became bedridden. A soft tumor of the back was accidentally discovered in June, 1918, located between the scapulae at the point where the pain was first noticed.

Examination.—Total paralysis of lower extremities and of abdominal and lower thoracic muscles. Marked knee and ankle clonus and positive Babinski sign. Legs extremely rigid and involuntary movements are caused by the lightest touch. Upper extremities and cranial nerves normal. Loss of all sensation below the level of fifth rib. A palpable tumor in back muscles, 1 cm. to the left of the fourth and fifth thoracic spines. Spinal fluid under low pressure, clear; cell count, 10; Nonne-Apelt globulin test, weakly positive; Lange test, weakly positive (0112211000). Examination of viscera negative. No glands palpable. Rectal and vaginal examination negative, except for a slight rectocele. Appearance of patient suggestive of anemia, but blood examination showed hemoglobin, 81 per cent.; red blood cells, 4,540,000; white blood cells, 9,100; blood pressure, systolic, 120, diastolic, 80. Roentgen-ray examination of the spine negative.

Operation.—A diagnosis of probable extramedullary tumor was made and the patient referred to Dr. Davis for operation, which was performed on Jan. 27, 1919. The tumor of the back was of a glistening appearance, measured 6 by 3.5 cm., and could be traced down to the intervertebral foramina above and below the fourth thoracic vertebra. After removal of the laminae of the upper five thoracic vertebrae the tumor tissue was found to be continuous with an extradural growth 4.5 cm. long, 1.7 cm. wide and 1 cm. in thickness, located posteriorly and to the left of the cord. It was readily peeled off, leaving the dura perfectly smooth.

Histologic Examination.—This was made of several intraspinal and extraspinal parts of the tumor. On account of the unexpected appearance, sections were submitted to Prof. E. R. LeCount, who stated that the tissue was mainly lymphoid in character and that the tumor belonged in the class of lymphosarcoma—of the same histologic character as the kind described by Kundrath and later by MacCallum.

Subsequent History.—In spite of the surgical success of the operation the patient failed to show the hoped for improvement. Although she was kept on a water bed, very extensive bedsores developed. The rigidity of the legs diminished rapidly and after a few days the complete picture of a total transverse lesion existed, all of the reflexes being lost below the level of the lesion. The patient also developed a bronchopneumonia, and died on March 7, 1919. No necropsy was obtained, so it could not be determined whether any lymphomatous tumors existed elsewhere in the body.

CASE 2.—*Summary.—Paraplegia of one year's standing with prolonged remission; loss of all sensation below eighth thoracic vertebra; legs spastic; little pain; removal of extradural fibroma followed by slow but steady return of motion and rapid return of sensation.*

History.—A boy, aged 15, gave a history of having developed an almost complete paralysis of both legs during the summer of 1917. At the time there was some pain in the lower chest on both sides, but no sphincter disturbance. The paralysis lasted only a month. In the spring of 1918 the symptoms gradually returned and by the beginning of October both legs became paralyzed and spastic. Only slight pain was complained of.

Examination.—Made on admittance in November, 1918: Spastic paralysis of both legs with great rigidity whenever limbs are handled. The upper thoracic muscles contract. Beevor sign present. Bilateral Babinski sign, knee and ankle clonus. Abdominal and cremasteric reflexes absent. Loss of touch and pain sense total below costal margin and relative below level of sixth rib. Roentgen-ray examination of the spine negative. The spinal fluid gave a negative Wassermann test, cell count 7, weakly positive Nonne-Apelt and Lange test (0112110000). A brief course of antisyphilitic treatment was given without any benefit. A tentative diagnosis of spinal cord tumor was made and the patient referred to Dr. Davis for laminectomy, which was made on Dec. 19, 1918. An extradural tumor, of the size of the end of the thumb, at the level of the seventh thoracic vertebra was readily removed. The tumor was found to contain a cavity partly filled with clotted blood.

Histologic Examination.—This proved the tumor to be a fibroma.

Subsequent History.—The patient soon regained sensation and after three weeks slight return of voluntary motion in the left toes was noted. From that time on return of power has been fairly rapid, but the patient is still unable

to walk and the legs remain quite spastic. It was thought that the hemorrhagic cavity in the interior of the tumor might explain the two separate attacks of paraplegia.

DISCUSSION

Dr. Peter Bassoe reported that the two patients operated on for extradural fibroma compressing the cord, shown to the Society by him in December, 1914 (J. Nerv. & Ment. Dis. **42**:736, 1915), were well. In case 1 there had been no recurrence. Case 2, the patient with the large hour-glass tumor partly outside the spine, developed weakness in the legs four years after the operation and in January, 1918, Dr. Dean D. Lewis again operated, removing all visible portions of tumor. The patient again made a perfect recovery.

Dr. H. N. Moyer cited a case operated on fifteen years ago by Dr. Bevan, which proved to be an exostosis at nearly the same level, with practically the same symptoms. It was about the size of one's thumb and compressed the cord into the form of a ribbon. The symptoms had been gradual in their onset, there being three or four years from the first weakness of the legs until the final, complete paraplegia set in. The tumor was chiselled away and the spinal canal restored. He had seen the patient a few weeks ago and there had been no recurrence of the growth. She still walked with a distinctly spastic gait, with a tendency to tilt a little on her toes. There was no incoordination or disturbance of feeling by usual clinical tests. The patient said improvement after leaving the hospital, continued for a little more than a year and a half, when she reached about the present stage. There were no fatigue symptoms whatever on walking and she had married and become a mother.

THREE CASES OF GLIOMATOUS CYST OF CEREBELLUM, WITH PRESENTATION OF SPECIMENS. Presented by Dr. George B. Hassin.

Case 1.—*History.*—A gliomatous cyst of the cerebellum is a variety of so-called cerebellar cysts. The latter are roughly classified by the English neurologist—Williamson—as cystic tumors and so-called serous cysts. In the former a cyst is always associated with a tumor, while in a serous cyst no vestiges of a tumor growth can be found. The first of my cases concerns a boy, aged 17, who entered Cook County Hospital on April 14, 1917, complaining of headache, vomiting and vertigo. The headache had started six weeks previously, without any apparent cause, was confined to the occipital region and was continuous. Vomiting had persisted for three days, about from ten to twelve times a day, always associated with dizziness.

Examination.—This showed a well nourished boy lying on the left side with the head and legs bent. Any other posture would induce vertigo and vomiting. The mentality, reflexes, general sensibility, abdominal organs, the genitals and the chest organs were normal. The *right* side of the face, lower half, was slightly paralyzed, the tongue deviated to the right; ocular movements and pupils were normal. The right disk was slightly blurred; the left, normal. Roentgen-ray examination of the skull, examination of urine, and serums showed nothing abnormal. The patient died about five weeks after he entered the hospital, the entire duration of the symptoms having been about three months.

Necropsy.—This revealed in the left cerebellar hemisphere, a small glioma, the size of a bean, very vascular and hemorrhagic, surrounded by a cyst. The latter contained about an ounce of sterile hemorrhagic fluid. The larger por-

tion of the cerebellar lobe was destroyed, the vermis pushed to the right and appeared compressed. The right cerebellar lobe was normal. The cerebral tissue showed no changes. There was no hydrocephalus.

The postmortem findings demonstrate that the symptoms could not possibly have been caused by the glioma, as he took sick suddenly and the entire duration of his illness was only about three months. Evidently he had long harbored a symptomless glioma until a hemorrhage into the growth with subsequent cyst formation caused the severe subjective complaints.

Forced position in cerebellar lesions (in this case on the left) has been frequently described (Jackson, Gordon, Smith and others), being evidently due to the release from pressure of the fourth ventricle and of the opposite healthy side. The third interesting feature was the cranial nerve involvement (the seventh and the twelfth) which was also present in the other two cases.

CASE 2.—*History.*—Joseph D., aged 21, came under my care on July 17, 1918, complaining of continuous frontal headache of five months' duration, dizziness and vomiting. There was, besides, severe pain in the neck, total blindness (for two months), inability to walk and a history of two convulsions with unconsciousness.

Examination.—The patient was found in a fixed position, on the right side, semiflexed. The neck was rigid and painful on movement; the right sixth nerve and all the muscles of both the third nerves, except the levator palpebrae superioris, were paralyzed. The patellar and Achilles reflexes on the right were lost, pupils rigid to light and accommodation, pulse from 96 to 160. The fundi showed marked bilateral papillo edema. The mental state, sensation, speech and urine were normal. There was no ataxia, no tremor. Walking was impossible, partly from great weakness, partly from blindness. The patient died a month later in convulsions after a decompression operation. The necropsy showed a glioma in the left cerebellar hemisphere and a cyst involving the vermis and a portion of the opposite hemisphere. There was no communication of the cyst with the fourth ventricle, no hydrocephalus, or other changes in the brain tissue proper. The point of interest in this case, aside from the fixed position, was involvement of the ocular nerves, the third on both sides including the intrinsic muscles, and the sixth on the right.

CASE 3.—*History.*—Charles L., aged 34, a switchman, entered the nervous service on July 27, 1918, complaining of headache (one year's duration), dizziness, failing vision, salivation (one month), gait troubles and difficulty in talking.

Examination.—No abnormal postures. There were slight ptosis, protrusion of the eyeballs, bilateral papillo-edema, slight ataxia in the upper extremities, slight nystagmus, swaying gait, marked Romberg and dysarthria. The tendon reflexes were quite lively on the left side, the skin reflexes, except the cremasteric, were normal. The patient had several convulsions during the period of his illness. The serologic findings, heart, lungs and urine were negative.

Postmortem Examination.—Glioma and cyst of the lower half of the left cerebellar lobe, slight hydrocephalus in the left hemisphere.

COMMENT

The three cases exhibited similar lesions and clinically they were somewhat alike. In all of them, there was absence of the majority of the phenomena described in experiments on animals and by Babinski in cerebellar lesions in

man. Thus, there was no nystagmus (except slight in case 3), no asynergic or "demesured" movements, no adiadokokinesis, and even ataxia was not present in all cases. The regular manifestations were the subjective complaints (headache, dizziness, vomiting), papillo-edema, and the involvement of some of the cranial nerves. Neither the papillo-edema, nor the cranial nerve involvement has anything to do with the cerebellum; namely, they are not the result of the disturbed cerebellar function. The occurrence of the lesion of various cranial nerves in intracerebellar affections has been repeatedly reported in neurologic literature (Tooth, Patrick, Homburger, Rout, Kitchen and others), being generally looked on as the result of the direct or indirect pressure (Fernwirkung). For many cases such an interpretation of the cranial nerve paralysis may be true, but some cases could be more satisfactorily explained and understood in the light of experimental work on the cerebellum done by I. L. Meyers of this city and a member of this society, and also probably by Weed (Baltimore). As it can be gathered from their experiments, especially those of Meyers, a removed cerebellar lobe produces hyper- or hypoactivity of the corresponding cerebral hemisphere with the disturbances of neuro-muscular action as the result of the changed function of the brain. The regularity with which the cranial nerves are involved in cystic lesions of the cerebellum would strongly speak in favor of the conclusions arrived at by Meyers, from his remarkable experiments. The fact that in some cases of cystic or other cerebellar lesions signs of cranial nerve lesion may be absent is most probably due to the so-called compensatory function of the brain. Luciani states that animals even with extensive injuries to the cerebellum do not show, in the course of time, any clinical symptoms or signs whatsoever. Such animals will jump, and run, and play as if no damage had been done to the cerebellum. Babinski himself, points out the fact that a cerebellar lesion is sometimes accidentally discovered on the postmortem table without having been manifested clinically. Such compensatory functions of the brain must necessarily occur in older cases in which no cranial nerve involvement may be found. Recent cases, however, like the ones under discussion and as it can be gathered from the literature show this phenomenon with remarkable frequency and regularity.

DISCUSSION

DR. I. LEON MEYERS thought while a few of the symptoms in Dr. Hassin's case could be explained in accordance with his ideas of the cerebellar functions, others must be looked on as indirect symptoms. Regarding the deep reflexes, if we assume that the cerebellum exerts an inhibitory effect on the higher cerebral centers, the cause of their diminution or loss is of course obvious.

In the first case the patient was lying on the left side. This is a minor form of the rolling movements to the left, observed in animals and must be explained, in his experience, as indirect symptoms. He had pointed out some time ago that forced movements were not cerebellar symptoms, regardless of the numerous statements to the contrary. He had removed in a number of animals practically the whole lateral lobe of the cerebellum and they did not show any forced movements. They are constant, however, after lesions of the vestibular system. The animal after such a lesion, being more conscious of one direction than of the other, will of necessity turn its head and look in that direction and we have conjugate deviation of the head and eyes to the right or to the left as the case might be. In the comparatively large number of animals in which he observed rolling movements, conjugate devia-

tion of the head and eyes and allied phenomena, there was invariably a lesion of the vestibular nerve, the vestibular nuclei or posterior longitudinal bundle.

He had not made microscopic studies of the lesions. He could observe, however, that in small lesions the animal fell to one side, or turned its head to one side whereas in large lesions they turned around. He was convinced that the position in the case was due to some pressure on the left side. He thought the diminution of the reflexes was best explained by the theory that the cerebellum functionates as a checking organ on the motor centers of the cerebrum.

Dr. Peter Bassoe asked if the cranial nerve symptoms were not very frequently due to hydrocephalus. In many cases of cerebellar tumor there had been so much hydrocephalus that it was easy to explain the involvement of the cranial nerve by the stretching of the nerves from the downward pressure.

Dr. Hugh T. Patrick was of the opinion that cranial nerve involvement in tumors and cysts of the cerebellum was to be accounted for on mechanical grounds.

Dr. George B. Hassin, in closing, said he wished to point out the regularity with which the cranial nerves were involved in cysts of the cerebellum, especially in cases not advanced. He did not agree with the explanation given by Dr. Meyers regarding the abnormal position of the body. The forced position of a patient with a cerebellar cyst was not the result of a disturbed cerebellar function, being rather a matter of comfort for the patient. He feels less distressed when lying on the diseased side, as a position on the healthy side causes increased pressure on the aqueduct of sylvius and greater distress.

The hydrocephalus could not be considered the cause of the multiple nerve involvement, because out of the three cases demonstrated only one showed a hydrocephalus which was unilateral and very slight. On the other hand, a regular cranial nerve involvement did not occur in hydrocephalus associated with other brain lesions.

As cerebellar cysts usually bring about an extensive and even complete destruction of whole lobes of the cerebellum, they could be utilized for the purpose of studying the clinical symptoms resulting from such a destruction. Solid tumors were less adapted, as they usually leave a larger portion of the cerebellar tissue comparatively intact.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, March 20, 1919

George A. Waterman, M.D., *President*

A NOTE ON DR. SOUTHARD'S ORDER OF EXCLUSION IN DIAGNOSIS. Presented by Dr. Lawson G. Lowrey.

Dr. Lowrey stated that in mental diseases there is no definite system of presenting symptoms, but in considering any one case it is possible to narrow the possible diagnoses down to two or three groups. Dr. Southard has presented a scheme of diagnoses that contains eleven groups. Another possible order of grouping is one based on statistical frequency. This method would

result in different orders in different institutions, and is therefore objectionable. A better basis is one founded on etiologic factors.

Dr. Lowrey agreed with Dr. Southard as to the first four groups: the syphilopsychoses, the hypophrenoses, the epileptoses, and the pharmacopsychoses. In the last five groups, he also agreed: the geriopsychoses, the schizophrenoses, the cyclothymoses, the psychoneuroses, and the psychopathoses. As a fifth group, Dr. Southard has the encephalopsychoses, and as a sixth group the somatopsychoses. Dr. Lowrey thought that a reversal of this order is clearer, more logical, and simpler for teaching. He therefore suggested that the fifth group should be the somatopsychoses, and the sixth group the encephalopsychoses.

DISCUSSION

Dr. Elmer E. Southard stated that the grouping that he had made was not based on a teaching consideration, but on reliability of tests of differentiation. The first four groups are social groups, the fifth concerns the neurologists, the sixth the problems of internal medicine. Such a grouping has the disadvantage of bringing into juxtaposition certain cases that might better be more widely separated. He had considered the order that Dr. Lowrey suggested and recognized the arguments for the transposition. The exact sequence of the grouping he thought less important than the acceptance of a definite classification.

A CASE OF ENCEPHALITIS LETHARGICA. Presented by Dr. Charles A. McDonald.

A case reported in brief and diagnosed as encephalitis lethargica, showing signs characteristic of this disease as described by Von Econimo, Netter and Smith. The patient had cranial nerve involvement as shown by ptosis and diplopia. The lethargy was the initial and presenting symptom—mild at first—increasing in severity until she was comatose before death. Until the last two days of her illness she could be roused when she would be found to be oriented. In addition she had absent deeper reflexes. No Babinski sign. No bladder disturbance. White blood cell count a little less than 10,000 and spinal fluid within variation. Necropsy showed a general increased vascularity with no evidence of meningitis.

THE QUESTIONS OF DURATION OF ATTACK AND RECURRENCE IN MANIC-DEPRESSIVE INSANITY. Presented by Dr. John B. MacDonald.

The problems of prognosis, duration of phase, length of interval, and recurrence in manic-depressive insanity were considered; also the light thrown on these problems by a study of 450 cases of this disease at the Danvers State Hospital. As to age periods, thirty-six males and eighty females, totaling 116, or 25.7 per cent., were 25 years or younger in age. Forty-four males and 132 females, totaling 176, or 39.1 per cent., were mature, namely, 25 to 40 years old. Forty-seven males and 100 females, totaling 147, or 32.5 per cent., were climacteric, that is, 40 to 60 years old. And four males, and eight females, totaling twelve, or 2.3 per cent., were postclimacteric, that is, 60 or more years old. Depression was the most frequent initial phase, being nearly twice as

common as manic or mixed types. When the initial attack was depression the second attack recurred with men in about 10.6 years, and with women in 10.9 years, but with an initial manic or mixed attack the average interval of recurrence in men was 6.1 years and in women 6.5 years.

On the other hand, the average duration of attack was considerably longer in the depressed cases. Only 62 per cent. of the depressed cases discharged recovered in six months, while 79 per cent. of the manic cases were so discharged. The recovery curve for manics reached its height between the fifth and sixth month; for depressions, between the seventh and eighth, when the initial attack occurred below the age of 40.

Beyond the age of 40 permanent recoveries were rare from first attacks. Apparently it is most difficult for the manic-depressive case occurring after 40 to realize that he has passed the zenith of his powers, and that his plane of accomplishment is on a lower level.

In 295 of the 450 cases recurrences occurred. In 100 cases all the attacks were of the depressed type; in 128 all were manic.

To gain an idea of the tendency toward establishment of the complete manic-depressive cycle, a review was made of 100 cases in which the completed life history was known. Of these, seventy-eight showed in one or more attacks a variation of type, namely, a completion of cycle; twenty-two presented attacks of one general type throughout, but differing in duration and intensity. Of those showing uniformity of phase in all attacks almost two thirds were depressions.

In the case of depression, the extremes of duration of free intervals after first attacks varied from forty-four to two years for females and twenty-eight to two years for males. Following initial manic attacks, the extremes for females were twenty-eight and two years, and for males thirty-nine and one years.

Between the extremes mentioned, individual cases presented a bewildering variation of interval durations. Given certain antecedents, certain consequences do not uniformly follow in manic-depressive disease.

DISCUSSION

Dr. H. R. Stedman asked the reader as to how many cases of recurrent paranoid conditions he had seen. He also asked regarding seasonal variations, and the possible influence of the season as a factor governing the recurrence.

Dr. E. B. Lane stated that he had seen cases that completed a double cycle in a year. Environment played little part in the production of the condition. He thought that some somatic factor played a decisive part.

Dr. E. E. Southard asked whether the analysis shed light on the problem as to whether manic-depressive insanity is a psychosis or a group of psychoses. Is Kraepelin to be credited for a new disease or merely a synthesis of disease? Would a study of heredity help?

Dr. MacDonald (closing the discussion) said that many of the cases did not seem to be distinct entities. He thought that the condition was probably a group of conditions. Completion of cycle was shown in seventy-eight out of 100 cases.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 28, 1919

J. HENDRIE LLOYD, *President*

A CASE OF HEMIHYPERTROPHY. Presented by DR. J. W. MCCONNELL.

D., 7 months old, was born prematurely, but except for the fact that she was a seven months' child, was apparently normal. She was breast-fed and seemed in no way to be out of the usual, until at 2 months her mother noticed some difference in her lower extremities, this difference consisting of an unusual fatness of one leg as compared with the other. This condition has continued and has somewhat increased up to the present state.

The family history shows nothing important as to the father. The mother has had four pregnancies altogether, two of which were abortions; another was a child who is now 4 years of age, and the fourth is the patient of whom we are speaking. We found on examination a very marked asymmetry, our opinion being that the left side of the body was the pathologic one, this opinion being based on the appearance on the external surface of the leg of an unusual development which simulated a mass, the right leg not showing anything at all like it. The whole lower extremity, the buttock, the left labium, the left arm and slightly the left face, were quite larger than the corresponding members of the right side. There was little or no asymmetry of hands or feet.

This enlargement was smooth, firm to the feel yet not hard, was in no way boggy or edematous. There was no change in the color of the skin. The superficial blood vessels were not in any way dilated, and the surface temperature was the same as that of the right side. There was no loss of power and, so far as one can judge in a 7 months' old child, no incoordination. The tendon reflexes were present and apparently normal. The child was quite as intelligent as one would expect for the age, and otherwise than as indicated was perfectly normal.

The other living child in the family was between 3½ and 4 years old, was very large, weighing 51 pounds; the lower extremities were symmetrical, very well developed to the point of the suspicion of hypertrophy. There was no paralysis, but the knee jerks and Achilles jerks were not obtained.

The enlargement from roentgen-ray studies seemed to be entirely confined to the soft parts, as can be seen from examination of the roentgen-ray plate; the bones on both sides of the body were the same size—longitudinally and transversely—and the shadows of the soft tissues were no denser on one side than on the other.

TRANSVERSE MYELITIS IN A CHILD WITH THE ABSENCE OF THE TOE-PHENOMENON BY BABINSKI'S METHOD BUT PRESENCE BY OTHER METHODS. Presented by DR. ALFRED GORDON,

Boy, aged 9, presents evident signs of rickets: Scoliosis, one scapula larger and thicker than the other; curved tibia with convexity forward on both sides, more pronounced on the right. Prior to December, 1918, he was apparently in good health. At that time he complained of stiffness of the neck, became languid and apathetic. Rapidly he developed a weakness in the legs and had difficulty in walking. At the same time difficulty of micturition made its appearance.

At present the paralysis is not complete, as the patient is able to stand up when supported and to move his limbs when in bed, more on the left than on the right side. The knee jerks are increased on both sides. Ankle clonus is present and very marked on both sides. Babinski is absent on both sides, but the paradoxical reflex is present and distinct on both sides. Oppenheim's reflex was also distinct on both sides, but presently is obtainable only at times. Shäfer's sign is persistently present. Sensations to touch and pain, also temperature, are diminished from the toes up to the knees. The cremasteric reflex is much diminished on the left side. The sphincter of the bladder is disturbed: from retention the condition changed to imperative micturition.

The literature abounds in examples of this kind. There are cases in which irritation of the plantar surface produces extension of the great toe, but pinching the thigh and abdomen produces flexion of the same; cases of paraplegia, such as reported by Almeida and Espozel, in which Babinski's sign is positive, but negative after Esmarch's band had been applied and then removed; cases in which at first there was flexion and immediately afterward extension of the big toe. This phenomenon was observed in cases of cerebrospinal meningitis, of Brown-Séquard's paralysis, in cases of a lesion at the level of the seventh cervical vertebra. Guillain and Barré observed flexion in the ventral position and extension in the dorsal position of the patient. Landau of Switzerland, in a recent contribution (*Presse médicale*, 1917), reports a large series of cases in which the above-mentioned variations of response in the great toe or all the toes have been evident. He concludes with the following remark: The procedure of producing extension of the great toe is not single; not only it varies from one individual to another, but it may happen that while all methods may be positive in one individual, only one may be present in another. In one case Gordon's method may give extension, while all other methods may be negative, etc. One cannot say that the toe-phenomenon is absent unless all methods have been used."

A CASE OF DISSEMINATED SCLEROSIS (?) WITH ASTEREOGNOSIS. Presented by Dr. Alfred Gordon.

A man, aged 23, laborer by occupation, commenced to feel various paresthetic disturbances, also developed a tremor in his fore limbs. The tremor disappeared at the end of several weeks, but the paresthesia remained. Six months ago he commenced to suffer from headache and diminution of vision, also from pain in the legs.

Examination reveals a fairly well-advanced secondary optic atrophy in the right eye (the left eye was enucleated in childhood). Pupil is normal. Visual acuity 8/200. The visual field is not contracted (Dr. LeFever). The gait is somewhat spastic. Ankle clonus on the left. Babinski on both sides. There is occasional incontinence of urine at night. Sensations: Superficial sensibility (touch, pain and temperature) is intact. The deep sensibilities are intact with exception of compass sense and stereognostic sense: at a distance of about 2 inches the two points of the compass begin to be distinguished as separated points; below that space, as one single point. Astereognosis is distinct and marked, especially for small objects, in the left hand, and sometimes there is difficulty of recognizing objects placed in the right hand. The senses of position and pressure are recognized by the patient. It seems, therefore, that stereognosis is not dependent on superficial and other deep sensibilities, but it is a sense apart. Moreover, the patient is fairly well able to recognize the form and consistence of objects, but is unable to name them. Asymbolia, therefore,

must be dissociated from astereognosis, which deals only with form and consistence of objects. The patient gave no history of venereal infection and the Wassermann reaction is negative.

As to the diagnosis, in spite of the absence of nystagmus and staccato speech, multiple sclerosis forces itself. We probably deal here with disseminated foci of sclerotic nature in various portions of the central nervous system. The optic atrophy, the astereognosis (pointing to the parietal lobe), the spastic paraplegia—all indicate the probability of the disseminated sclerotic processes.

CEREBRAL SYPHILIS WITH BILATERAL SEVENTH NERVE PALSY AND INVOLVEMENT OF THE EIGHTH NERVES. Presented by Dr. J. Hendrie Lloyd.

Dr. Lloyd's interest in syphilis of the nervous system has led him for some time to look particularly for involvement of the eighth nerves and apparatus of hearing, because syphilis of the auditory nerve and labyrinth is not so uncommon as once supposed. At a former meeting of this society he reported a case of almost total deafness coming on very acutely a few months after the primary sore, and due doubtless to a syphilitic lesion of the auditory nerves.

Dr. Lloyd presented two other cases, the auditory tests in which were demonstrated by Dr. Lewis Fisher.

Case 1.—This case is particularly interesting, because the patient presents also a bilateral seventh nerve palsy, which is in itself a rarity. This patient, a colored man, aged 23, had a primary sore in September, 1918, and was admitted in October to the venereal wards of the Philadelphia General Hospital. He was given two doses of arsenobenzol, and left the hospital on December 1 against advice. There was no record at this time of any involvement of his nervous system. About three weeks later (December 24) he began to have severe and persistent headache, accompanied with vertigo and tinnitus in both ears. He staggered slightly, but at first there was no paralysis of the facial nerves. He was readmitted to the hospital about the first of the year, and at this time had well-marked paralysis of both facial nerves, more marked in the left. He had himself first noticed it from inability to hold a cigaret between his lips. The paralysis was of the peripheral type on both sides, involving the frontalis, the orbiculares, the upper and lower face and the lips. There has never been impairment of the third, fourth, fifth, sixth, tenth or twelfth nerves on either side. Taste and smell were not affected. There was no evidence of involvement of the cord, either in sensation or motion, but the knee jerks were unequal and the Achilles jerk on one side (the left) was totally abolished. The pupillary responses were normal: no optic neuritis. There was no dysuria. The laboratory reported on several specimens that the Wassermann tests for the blood and spinal fluid were positive, and globulin positive. At first the cell count was as high as 780—but later this had fallen to 36 per cubic mm. under treatment. He received six doses of arsenobenzol to date (March 21). Dr. Byrne reported a slight obstructive deafness. The positive but shortened Rinné with loss of intermediate notes, pointed strongly to involvement of the nervous mechanism. Dr. Lewis Fisher reported total absence of response to douching and turning, which would indicate a peripheral or eighth nerve lesion; but a definite presence of vertigo after turning, as well as preservation of a fair amount of hearing on both sides, shows that the nerves in their entirety were not involved; and he suggested a bilateral syphilitic lesion of the brain-stem on the mesial aspect of Deiter's nucleus, thus allowing for the

escape of the fibers for vertigo and most of the auditory fibers. The difficulty of excluding a purely peripheral lesion was the fact that both seventh nerves were implicated along with the eighth nerves. A syphilitic meningitis or neuritis, involving both the seventh and eighth nerves, would seem a probable lesion —and the fact that not all the cochlear-vestibular fibers were involved, but only some of them, would be in accord with what we know of the selective, or erratic, action of the spirochetes.

CASE 2.—*Cerebral Syphilis with Eighth Nerve Involvement.*—The second case was that of a Russian, aged 48, who was admitted to the venereal wards on Sept. 5, 1918, with a primary sore. He received mixed treatment and five doses of arsenobenzol. In December the sore was still unhealed, and there was enlargement of the lymph glands of the groin and neck. In March the patient began to complain of inability to walk straight. He staggered and fell to the left. Trouble with hearing had commenced earlier in the right ear, in which he had become quite deaf. Progressive deafness was later present in the left ear. There was loud tinnitus in the right ear, which kept him awake at night. The Wassermann test of the blood was reported negative, but the spinal fluid was positive ++++. A curious phenomenon was complete abolition of one Achilles jerk (the left), just as in the other case. The knee jerks were free, especially the left. There is a low-grade double optic neuritis. The frontalis muscle on the left was smoothed out, but the orbicularis was not involved, nor the facial muscles, unless very slightly. The pupils reacted normally to light and on accommodation. All the other cranial nerves were normal. The pain, temperature and tactile senses were normal throughout. The gait was staggering, not ataxic, and there was a slight Romberg sign. Dr. Fisher found by testing that the right labyrinth was completely, the left partly, involved. There were no reactions to turning or douching. The case seemed to be a clear one of peripheral involvement, that is, of the labyrinths and eighth nerves in both branches.

It was a curious coincidence that both of these patients presented a unilateral absence of the Achilles jerk—without other marked evidence of involvement of the spinal cord. The explanation of this was not apparent, unless it meant slight beginning changes in the posterior columns or nerve-roots. But otherwise there was no evidence of tabes.

DISCUSSION

DR. LEWIS FISHER stated that he did not wish to be understood as disputing the diagnosis of Dr. Lloyd. He did, however, state to Dr. Lloyd in his report that from the ear standpoint he could not explain one of the cases presented on the basis of a peripheral lesion pure and simple. He demonstrated the reasons for his opinion when he examined the two cases in the turning-chair in the presence of the Society. Although the normal responses obtained from labyrinthine stimulation by turning were well known and accepted for a number of years, this war has offered an unusual opportunity for verifying them. An examination of some 60,000 prospective aviators in the Army has definitely shown that every normal individual had nystagmus of twenty-four seconds average duration after ten turns in a revolving chair. He simultaneously also experienced a vertigo—that is, a sensation of turning which is not in accord with fact—lasting between twenty-five and thirty seconds after ten rapid turns in a revolving chair. These phenomena are explained in the following way: When an individual was turned in a chair which was suddenly brought to a standstill, the lymph within the semicircular canals

of the labyrinth continued circulating by sheer force of momentum imparted to it by the turning. The moving lymph impinged against groups of ciliated hair-cells placed on little mounds at the ends of the semicircular canals. Just so long as this lymph continued moving, just that long there appeared the two responses noted—namely, nystagmus and vertigo. Both of these responses, therefore, originated within the labyrinth. The eye-movement impulse has the posterior longitudinal bundle for its destination. The vertigo impulse, which is a conscious sensation of motion, naturally, has the cerebral cortex for its destination. Each impulse travels very likely along a nerve-pathway of its own. All of these pathways are together within the eighth nerve. After the eighth nerve enters the brain-stem, where it breaks up into its constituent portions, these responses take different courses. Whenever there is a peripheral lesion within the labyrinth it usually affects *all* the ciliated hair-cells. It would be improbable for the pathologic process to destroy one set of hair-cells and leave the other set absolutely intact. The same is probably true of a lesion involving the eighth nerve itself. This uniform and proportionate involvement of all the responses is the distinctive feature of a peripheral lesion. When we say all the responses we also include the hearing. There have been observed, however, several cases of undoubted peripheral lesion where the hearing was not affected while the vestibular responses were practically absent. The association, however, of the auditory fibers with the vestibular fibers, although intimate, is not quite as intimate as of the two sets of vestibular fibers. This might explain the few exceptions.

In the case referred to (that of the colored man) we have the following findings. His hearing was quite good on both sides. When he was turned in a chair there was absolutely no nystagmus or eye-response, but there was present almost normal vertigo. The fact that vertigo was present indicated that the lymph was set in motion by the turning. How will it be explained then that this circulating lymph stimulates one set of ciliated hair-cells—namely, those for vertigo—and not the other? If the syphilitic toxin affected the labyrinthine contents themselves it would be unlikely for it to destroy the eye-movement fibers to utter extinction and leave the vertigo fibers practically intact. A more likely explanation of this phenomenon is that the pathologic process affected the eighth nerve distribution at some point where the eye-movement fibers have parted company from the vertigo fibers—namely, in the brain-stem. If our conception of the vestibular nerve-pathways be correct such a lesion would have to be bilateral in the region of Deiter's nucleus. This is purely an otologic suggestion to the neurologist and is offered only with the thought that it might fit in with the general neurologic picture, which this case presented. If the other general neurologic evidence points unmistakably to a peripheral lesion, probably the neurologist will help to explain these perplexing otologic data.

Another thought that was offered was this: Since it is well known that syphilis has a predilection for eighth-nerve tissue, could it not be possible that in this particular case the toxin had affected this eighth nerve distribution at more than one point—both peripherally and centrally? If this were true then everything could be easily explained.

The other case showed a marked impairment of *all* responses—hearing as well as nystagmus and vertigo. This was fully in conformity with the usual ear-findings in a case of peripheral lesion and the otologic examination simply corroborated the neurologic data in this case.

DR. GORDON asked Dr. Fisher whether he used the electrical current in examination of the vestibular apparatus; to which Dr. Fisher answered in the affirmative.

DR. GORDON asked him to tell the Society the comparative results between the two types of tests.

DR. FISHER replied that galvanic stimulation in vestibular cases was not generally employed for the reason that the electric current penetrates the tissues and stimulates, not only the hair-cells within the labyrinth, but also the nerve fibers within the eighth nerve and perhaps even the nuclei themselves within the brain-stem. In other words, it is an agency over which we have very little control so that the presence of a response on such stimulation does not indicate where the stimulus started. In some cases, however, it is very valuable, especially in those peripheral affections where there is a question whether the lesion is labyrinthine or retro-labyrinthine. In those cases it is the only means of differentiating between a lesion within the labyrinth itself and the eighth nerve.

DR. MILLS said he positively could not see why it could not be just at the junction of the fibers with the brain-stem. Omitting the Bárány tests the symptomatology seemed to be that of peripheral cases.

DR. FISHER responded that was the way it seemed to him.

DR. LLOYD stated he only wished to reiterate that he thought the simplest explanation of the first case was a syphilitic meningitis involving the seventh and eighth nerves on both sides where they emerged from the brain-stem. In support of this view it is known from other observers that syphilis of the eighth nerve is nearly always bilateral, and that it does not always involve all the fibers of the nerve, but sometimes only some of them. Thus the vestibular root alone may be involved, or in other cases the cochlear root alone. This selective action of the organism of syphilis is not unusual.

CEREBELLO-BULBAR POLIOENCEPHALITIS ORIGINATING DURING OR AFTER EPIDEMICS OF INFLUENZA AND OF POLIOMYELITIS, INCLUDING THE RECORD OF A CASE OF EPIDEMIC ENCEPHALITIS OF THE LETHARGIC TYPE. Presented by DRS. CHARLES K. MILLS AND GEORGE WILSON.

This paper was published in full in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY **1**:567 (May) 1919.

A CASE OF LETHARGIC ENCEPHALITIS. Presented by DR. P. N. BERGERON.

The patient was a single man, aged 34, formerly employed as a chauffeur, but lately engaged in automobile repair work. The family history may be of some interest; a brother died at the age of 19 years, after a short period of illness; his case was diagnosed "water on the brain" (this occurred about twenty years ago). The parents are both dead. The cause of death in either case cannot be now ascertained. There is a sister still living and in good health.

During the past eight or nine years, the patient suffered from a few attacks of rhinitis and pharyngitis. About two years ago Dr. Bergeron operated on him for lipoma of the cheek. Previous to last October the patient had had no serious illness. In October he fell a victim to the then prevalent "grippe," which disabled him for a period of ten days. This attack was not followed

by any serious complications, although he did complain of a slight pain in the loin; this pain gradually disappeared in a few weeks. After that he enjoyed good health.

March 8: The patient arose as usual, but soon discovered that his vision was so impaired that it was impossible for him to read. This, however, did not alarm him at the time. Two days later he complained *only* of this partial blindness.

Examination of the eyes showed that vision was 20/40 in both eyes. The eye ground presented a congested appearance at the nerve heads. His temperature was normal, and the pulse was 86. By close questioning it was brought out that he felt more dull than usual, but did not feel ill. Test for the reaction of the tendon reflexes showed no abnormalities. There was no paralysis, nor muscular weakness. The tongue was projected normally, and was covered with a heavy white coating.

March 13: The patient was unable to leave his bed. His condition grew steadily worse, and he was taken to St. Mary's Hospital. He lay on his back in bed, his legs fully extended, the arms flexed across his chest, his eyes closed and he was apparently sleeping. When asked, "How do you feel?" he would reply, "Good, but dull." He spoke slowly but intelligently, and immediately relapsed into an apparent sleep. He would remain in this condition until spoken to again. All the reflexes were normal, except the pupillary reflex, which was very much slower than on the previous day. When asked to open his eyes, voluntary effort on his part was fruitless. If the eyelids were lifted by the examiner and held so for a few moments, the patient would subsequently open them if spoken to, but soon closed the eyes again. The tongue was projected with difficulty, the lips were parted with marked effort on the part of the patient. When asked if he recognized the persons who were around his bed, he answered in the affirmative.

The temperature was 100 F., and the pulse was 86.

March 14: The condition of the patient remained unchanged. However, at this time it was noticed that the bowel and the bladder were incontinent. The patient was seemingly unaware of this. The sleeping was accompanied by snoring. The nurse observed that the patient had frequent attacks of tremor of the whole body that shook the bed on which he was lying. The temperature was 100 F., and the pulse was 86.

March 15: The condition of the patient remained much the same as on the previous day, except that he seemed more lethargic. It was also noticed, for the first time, that the arms and legs were rigid, and it required an effort on the part of the examiner to flex them. There was no voluntary movement of the eyes. The eyelids remained closed, unless lifted by the examiner. It was noticed that the right eye could not move toward the right and showed an apparent internal strabismus. Pupillary reaction was very sluggish and the pupils were irregular. The head moved easily in all directions, showing that apparently there was no rigidity in the muscles of the neck.

At this time the mental condition was very cloudy. If spoken to, his answers were unintelligible. When the spinal cord was tapped, he took no cognizance of it. Incontinency of the bowel and bladder still continued. The temperature was 101 F., and the pulse was 110.

March 16, 17 and 18: The condition of the patient during these days changed somewhat. He was not so sleepy as heretofore, he responded more quickly, and settled his business affairs, also questioned those who were around him. The rigidity of the arms and legs was more marked. The eyes opened

more easily. The weakness of the right eye had entirely disappeared. Vision did not grow worse. No rigidity of the muscles of the neck developed. The pupillary reflex seemed to quicken. There was no apparent difficulty with deglutition. The temperature gradually rose to 103 F., the pulse to 160, and the respiration to 60. On March 19, at 5:30 a. m., he died suddenly.

Urinalysis.—There was a trace of albumin, otherwise it was negative.

Blood Examination.—Red cells, 4,160,000; leukocytes, 12,400; hemoglobin, 85 per cent. Differential Count: Polynuclear leukocytes, 77 per cent.; large lymphocytes, 8 per cent.; small lymphocytes, 15 per cent. A culture made from the blood was negative. The Wassermann test of the blood was negative.

Spinal Fluid Test.—Fluid was clear, and it reduced Fehling's solution. Globulin was increased. Cell count was 13 cells per cubic millimeter. No bacteria were found. No growth found on culture. Wassermann test of the fluid was negative.

TWO CASES OF INTRACRANIAL INFLUENZA SEQUELAE. Presented by Dr. S. F. Gilpin.

Case 1.—G. C., a white man, aged 57, came to the clinic on March 12, 1919. He gave a history of always having good health until he had influenza during October, 1918. He was in the house two weeks, recovered and worked until January 3. During December he had sharp pains in the back of his head and neck and across the eyes. He was treated by an osteopath. During the night following the fifth treatment he felt queer in bed, arose and went down stairs. Here he became dizzy and could not walk. He was put to bed and vomited five times. He had double vision for one week after this. He complained of pain in the head and back of the neck and of paresthetic sensations well distributed over the body. He was unable to work.

Examination showed ataxia of both gait and station. Pupils were unequal and reacted slowly to light. No diplopia was seen. There was moderate ptosis of the right upper lid. According to Dr. Heed the central retinal vessels show the changes of arteriosclerosis. The patient had a tendency to choke when swallowing liquids. No palsy of muscles of throat could be determined by examination. Touching his left hand produced the sensation of heat to the patient. His sphincters were controlled. The blood and fluid Wassermann reactions were negative. The fluid showed 5 cells per cubic millimeter and an increase in globulin. Both smear and culture of the spinal fluid were negative.

Case 2.—This patient, A. K., was a white man, aged 25. He had a history of good past health until he had influenza last October. From that time he complained of weakness and nervousness.

For the past five weeks he complained of a pulling sensation in the eyes with severe headaches. He had noises in his ears like the boom of a cannon, like music, and like the singing of birds.

His physical examination was entirely negative with the exception of a primary optic atrophy. The blood and fluid Wassermann reactions were negative. He showed no cells and no excess of globulin in fluid. There was no knowledge of optic atrophy in this patient until his eye symptoms caused him to go to the Wills Eye Hospital a few weeks ago.

The question was the relation of the attack of influenza to the present condition of the nervous system in these two patients.

DISCUSSION

DR. ALFRED GORDON asked how soon after the influenza infection the present disturbance developed.

DR. GILPIN replied that they had influenza in October and in the one case the man went back to work in January. That was two months after the infection the symptoms developed. The other patient had influenza at practically the same time.

DR. WILLIAM G. SPILLER said he had seen three cases of lethargic encephalitis. He thought the case Dr. Smith had shown from his service at the University Hospital at the last meeting was probably of this type. That boy had entirely recovered.

A man, aged 43, was referred to Dr. Spiller by Dr. Shumway. About February 15 of this year diplopia developed suddenly. The man remarked that he saw double on looking out of the window. He had bilateral ptosis and weakness of all the ocular muscles, especially of the superior recti muscles. At this time he had slight headache and great drowsiness, and he soon became delirious. He would drop off to sleep at any time and it was difficult to keep his attention. If he were spoken to he would answer correctly and then would lapse into this peculiar mental state. If left alone he would talk to himself in a rapid low voice. He would talk in this way much of the night. There was no facial palsy at that time.

He showed the characteristic progression of cranial nerve palsy. On February 22, he developed weakness of the right side of the tongue. On March 3, a beginning paralysis of the right facial nerve was noticed, and within a few days this weakness became complete paralysis, and by this time the ocular palsies had disappeared. He had 42 cells in the spinal fluid to the c.mm., 96 per cent. of which were lymphocytes. The laboratory findings were those of syphilis, but he probably had had a syphilitic infection for years, and his acute symptoms were those of lethargic encephalitis in a syphilitic man. His temperature was 101 F. when he came into the hospital. He was well on the way to recovery.

The third case was from West Virginia. A man, aged 38, on Feb. 14, 1919, developed suddenly headache and nausea; following this he became very drowsy, he had diplopia, the retina in each eye became congested, and he was delirious. The diplopia improved after four or five days. He had a temperature of 101 F. He then developed a complete left facial palsy. When he came to the University Hospital he had free lacrimation and conjunctivitis, more marked on the side of the facial palsy. There was no rigidity of the neck and there were no signs of meningitis. Paralysis of the left cervical sympathetic nerve was present from the lesion of the left side of the medulla oblongata. Dr. Spiller expressed the opinion that there can be no doubt of the existence of sympathetic fibers in the lateral portion of this part of the brain. The sympathetic palsy was on the side of the facial palsy, but the sympathetic palsy predominated, and the palpebral fissure on the left side was smaller than that on the right. The sympathetic palsy has now disappeared. Dr. Shumway found the internal recti muscles were weak. The cerebrospinal fluid gave 9 cells to the c.mm. The findings were negative for the Wassermann reaction.

This man had been in a neighborhood where influenza had been prevalent. Dr. Spiller expressed the opinion that lethargic encephalitis probably would be recognized as a form of influenza, one in which the organisms were carried

from the nasopharynx directly to the brain, without causing gastro-intestinal or pulmonary symptoms.

In neither case was there involvement of the fifth nerve, and Dr. Spiller expressed the opinion that possibly this nerve would be found to be less frequently involved than were nerves whose nuclei were nearer the fourth ventricle or aqueduct of Sylvius. The findings in Dr. Wilson's sections showed that the lesions were more intense near these cavities. They resembled greatly those of the encephalic form of poliomyelitis, from cases of which Dr. Spiller had examined microscopic sections, but he did not believe poliomyelitis and lethargic encephalitis were identical.

Dr. Charles K. Mills said that what he had to contribute to this discussion had already been given in the paper by Dr. Wilson and himself. One thing that impressed him was the comparison to be made between the so-called lethargic cases reported here by Drs. Spiller, Potts and Dercum, and others, and the bulbar and pontile symptoms reported in the cases of Drs. Mills and Wilson. Omitting the lethargy, the bulbar and pontile symptoms were much the same in both the lethargic and nonlethargic cases. In four out of the five cases were marked cranial nerve palsies—seventh, sixth, third and, in one instance, fifth. Most of the cranial nerve symptoms tended to recover, as in many of the lethargic cases. Dr. Mills said that he believed one point was most interesting, the very last point referred to by Dr. Dercum, namely, that in the cases which have been recorded in the lethargic disease, the symptoms have come on in part late. This was equally true of the cerebellobulbar and pontile cases described in the paper by Drs. Mills and Wilson. Certain symptoms appeared and then partially subsided or disappeared, but returned with increasing severity after a variable time.

Dr. Edward A. Shumway said that as Dr. Spiller had reported fully on his second case, he would confine his remarks to the first one. The man, when he first came to Dr. Shumway, showed paralysis of his right external rectus muscle. It was often difficult to determine the exact muscles involved in these patients because of the pronounced lethargy, which interfered with the determination of the double images, on which the ophthalmologist depends for his diagnosis. He subsequently developed disturbance of the oculomotor nerves, the left eye being most affected at first, especially in its upward movement; later, however, the right eye showed more limitation of its upward movement. There was partial ptosis of both eyelids, constant lateral nystagmus, increasing when the eyes were turned laterally or upward, and normal movements of the pupils to light. Ophthalmoscopic examination showed some blurring of both nerve edges, with hyperemia of the nerves. Within a few weeks, the oculomotor muscle palsies had improved very materially, as Dr. Spiller had said. Dr. Shumway alluded to a case, which he had seen in the Lankenau Hospital, which seemed to be of the same type, although he had understood that Dr. Potts, who had also seen this case, had thought at first it was a case of cerebrospinal syphilis. The patient came to the hospital with complete ptosis on both sides. There was marked disturbance of the rotations of the eyes, with involvement of both the oculomotor and abducens nerves, and the eye-grounds showed some hyperemia of the nerve heads. The patient was markedly stuporous, lying for hours at a time in this condition, although he would rouse sufficiently to respond if questioned sharply. He gradually improved apparently, the eye movements and lid movements were better, but suddenly the temperature shot up, one evening to 107 F., his breathing became affected, and he died. Unfortunately, no post mortem examination could be obtained. Another case

followed directly on an attack of influenza, in a young girl. In this case, however, there was a simple external rectus paralysis, without lethargy, and the paralysis was improving. Similarly, one other case had been seen at the University eye clinic, with paresis of both external recti, following influenza, also without decided mental disturbance. Ophthalmologists had been struck forcibly by the great number of muscle palsies, which they had seen recently, which seemed to be associated with the epidemic of influenza.

Dr. Francis X. Dercum thought that the two cases presented by Dr. Gilpin were very properly referable to "grippe." Both presented organic changes suggesting encephalitis. Dr. Bergeron's very interesting case was another example. When Dr. Dercum saw this case the ptosis and inability of the patient to move the eyeballs freely and the sluggish reaction of the pupil to light were very striking. The man was very lethargic and somnolent, and ran a very moderate temperature; the whole picture at once suggested encephalitis lethargica. In a case which Dr. Dercum saw only a few days ago, a man, aged 42, and subsequently admitted to the Jefferson Hospital, a similar picture was present. There was a weakness of the eye muscles and lessened response of the pupils to light; and the mental condition again was one of somnolence and hebetude. At times this man was talkative at night, but soon dropped off and was again stuporous. A third case that Dr. Dercum had seen was still under observation at the Jefferson Hospital. Doubtless more of these cases will now be met with.

An especially interesting and important point was the extreme lateness of the development of the symptoms. Encephalitis lethargica does not seem to be a new and independent disease, but a sequel of "grippe." It would seem that in such cases the recovery which the patient makes from the initial attack is not a real recovery. Immunization has been incomplete, and later when the defensive reactions of the patient prove insufficient, the germs, again, gain the upper hand. The practical inference is that every patient who has passed through an attack of influenza, should remain in some degree under medical observation, should be full-fed, should be made the subject of a tonic and reconstructive treatment, and should not resume his occupation too soon. After encephalitis has occurred very little can be done for the patient. There is one point, however, which should be considered and that is whether drainage should be practiced. Dr. Dercum said that the drainage could do no harm and might do good; and he felt strongly inclined to urge it.

Dr. Charles S. Potts said that in reference to the case Dr. Shumway had mentioned as having been diagnosed cerebrospinal syphilis, he had seen the patient the day he was admitted to the Lankenau Hospital and suggested that it might be syphilis. After consideration Dr. Potts came to the conclusion that it was one of the cases of so-called lethargic encephalitis. The history of that man was of some interest, especially in view of what Dr. Spiller had said in reference to influenza. There seemed to be distinct relationship between the two as he had had influenza five weeks previously in one of the camps. He came home supposedly well and the first symptom of his attack was noted when he went to work, awoke one morning unable to open his eyes. He became stuporous and was sent to the Lankenau Hospital. He had no headache, no rigidity of the head and limbs and was intensely stuporous so that it was impossible to make a satisfactory examination of all the cranial nerves. Report on the condition of his eyes then stated that there was a third nerve palsy on each side, with ptosis, also paralysis of the fourth and sixth on one side, but that report said there was no evidence of optic neuritis. The cerebrospinal fluid was examined the next day and contained 76 cells—all lymphocytes—it

reduced Fehling's solution and was otherwise negative. He improved, became brighter mentally and the ocular palsy improved. On March 4 the fluid was again examined and was normal. The next day the patient became worse, the temperature rose to 107 F., the spinal fluid was examined again and contained 46 cells and in addition to the lymphocytes, contained a few polymorphonuclears, and it reduced Fehling's solution. He died shortly after that. Another symptom he had at the time Dr. Potts saw him was twitchings of the right side of the face. They could not make out any paralysis, but he had twitchings for several days.

Dr. Alfred Gordon said he had three cases which he wished to report. One case presented a temperature. The man in the very beginning had somnolence and then on the sixth day ptosis. There was also paralysis of the internal rectus of the left eye. The patient made a recovery in four weeks.

The second case was that of a woman, aged 27, who had a child with normal delivery; lochia normal. On the third day she developed a temperature of 104.1 F. and somnolence. She also had difficulty in swallowing and difficulty of speech because of awkwardness of the tongue. She presented involvement of the third, ninth and twelfth nerves.

The third case was a patient who showed temperature of 99.5 F., somnolence, palsy of the left external rectus, and difficulty in swallowing. In addition there was an anesthesia of the left cheek.

In all cases there was elevation of temperature. Whether it was "grippe" or not was difficult to determine, particularly in the case of the woman with the normal confinement, who suddenly developed high temperature. The three cases went into the category of lethargic encephalitis described particularly abroad. Encephalitis had been known for a long time. Accounts of its following infectious diseases can be found in the literature. Why should it be considered as a new disease? The disease has been known, but attention has not been particularly drawn to it. Netter wishes to consider it as an autonomous affection, but there is no substantial reason for it. In regard to the pathologic findings, Marie made exhaustive studies, and Dr. Gordon asked Dr. Wilson whether he also found lesions in the lobus niger.

Dr. Wilson replied that no lesions were found in the lobus niger.

Book Review

SYMPTOMS AND THEIR INTERPRETATION. By JAMES MAKENZIE, M.D., LL.D. (Aber. and Edinb.). Ed. 3, New York, Paul B. Hoeber, 1918.

Centuries ago a wise man propounded the theory that "of making many books there is no end," and as years were added to years this idea like many others expressed by him was amply verified. He put no qualification on the books, however, as to whether they would be good or bad, and it is not unreasonable to suppose that on a time a publication was handed to our much-suffering friend Job, who in the double capacity of invalid and critic, gave utterance to the famous "My desire is that mine adversary had written a book."

Were Job living today he would have accepted "Symptoms" most gladly and would have recommended it to his friends as a volume worth careful perusal. It is indeed a pleasure in these days of all kinds of literature to find a scientific book that can be read at will that is sufficiently practical to be interesting and of sufficient interest to make it readable without tremendous concentration of mind and consequent brain tire. The size of the book is comfortable to the hand; the topography easy to the eye; the text readily understood; the few illustrations quite graphic but hardly as happy as the occasional clinical pictures with which the 300 pages are interspersed.

The especial value of the publication is to the practitioner of general medicine who, although in constant touch with the development of a disease process, oftentimes undervalues some of the most important features or perhaps misinterprets them. To him the earliest premise of the book will be the keynote of the whole matter—"An inquirer should keep his mind free from bias and ready to review his most cherished beliefs." To be sure, we all may not accept the author's hypothesis as to the purpose of reflex symptoms—he admits the necessity for correcting some of his own pet theories; we may not all believe with him that "the pain of uterine contraction is a distinctly referred one," or that "a persistent pain along the supposed course of a nerve with tenderness on pressure often attributed to neuritis is not infrequently not due to neuritis, but is the reflex phenomenon arising from some diseased viscus," yet his arguments in favor of viscero-sensory and viscero-motor reflexes are most convincing and his clinical proofs are beyond immediate questioning. In evaluating symptoms the author emphasizes the need for the elimination of the neurotic habit induced by prolonged suffering before calculating the real importance of reflex phenomena. In a way, this is not new, but is worth having attention called to it.

One could analyze the book from each of its various chapter headings with many commendations and little fault-finding. Suffice it to say, that all through the volume the writer's premises are well founded, and his arguments are interesting and frequently unique and his deductions most valuable.